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**USSR Space Life Sciences Digest: Issue 24**
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## FROM THE EDITORS

This is Issue 23 of the USSR Space Life Sciences Digest. Of particular interest in this issue are abstracts of three chapters in a Soviet book on space immunology and an article describing the "Medilab" space station module (Operational Medicine: P1094, page 79). Other articles including space flight data are: Developmental Biology: P1092 (page 13); Endocrinology: P1109 (page 19); Neurophysiology: P1093 (page 73); Operational Medicine: P1096 (page 89); and Reproductive System: P1091 (page 98). Readers' attention is called to the Key Word Index, which has become a new feature of the Digest.

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**BOOK REVIEW:**

BR17(24/89) Agadzhanyan NA, Gnevushev VV, Katkov AYu.
Адаптация к гипоксии и биоэкономика внешнего дыхания.
Adaptatsiya k gipoksii i bioekonomika vneshnego dykhaniya.
[***Adaptation to hypoxia and the bioeconomics of external respiration.***]
Moscow: Izd-vo Universiteta Druzhba Narodov: 1987; 186 pages.
Reviewed in: Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 93-94; 1989.
Reviewer: I. I. Lanovneko

**KEY WORDS:** Adaptation, Hypoxia, Cardiovascular and Respiratory Systems, External Respiration, Voluntary Control

To a significant extent, adaptation to hypoxia determines the nature of the body's response to extreme conditions such as high altitudes, high latitudes, and arid zones. Such adaptation involves a regular compensatory response in the form of an initial increase in pulmonary ventilation. If a human has been adapted to extreme conditions for a sufficiently long period, a change takes place in the external respiration function. This change differs from that occurring in the initial stage of adaptation and involves a decrease in respiratory minute volume and an increase in oxygen utilization. To facilitate this adaptive process, we must develop a methodology that teaches subjects how to control external respiration consciously, enabling them to optimize this function by gradually decreasing its rate, and then helps them to automate this process. The research area known as "bioeconomics" [this term is used to mean efficiency and/or cost/benefit] of external respiration applies cost-benefit analysis and related principles to the problem of voluntary optimization of external respiration.

In this monograph, the authors cite their own experimental data and attempt to demonstrate that the principles of "bioeconomics" of external respiration can be used to facilitate human adaptation to hypoxia, alone and in combination with other extreme conditions.

The first chapter describes the current status of the problem of human adaptation to extreme conditions. The idea is expounded that adaptation to hypoxia is the central component of adaptation to the extreme conditions of high altitudes, arid zones, and high latitudes. This is most clearly manifest in the three stages of adaptation to high altitudes: the initial development of adaptation, which most often occurs during the first few hours at high altitudes; the emergency stage, followed by a transition period; and finally the stage of stable adaptation. The authors formulate the basic criteria for human adaptation to hypoxia, which ultimately reduce to attainment of the most efficient level of physiological functioning, not only at the systemic level, but at the cellular, subcellular and molecular levels as well.

Chapter 2, "The Bioeconomics of External Respiration," discusses data on the theoretical prerequisites for this direction in biomedical research, its structure, methodological approaches, and the parameters the authors use to evaluate the functional status of the body and, particularly that of the external respiration system. The authors introduce a technique for evaluating the efficiency of external respiration through use of an index called efficiency of external respiration (ELER). They demonstrate that voluntary optimal decrease in respiratory minute volume (VODRMV) exerts a beneficial influence on ELER parameters and on maximum physical and psychological work capacity, cardiac activity, and other parameters in healthy individuals and patients.

Chapter 3 describes the techniques for attaining VODRMV. The authors provide detailed recommendations for practitioners, discuss indications and contraindications, and cite results on the effects of VODRMV on the biomechanics of respiration in healthy individuals and patients, obtained through the use of spirographic analysis, and on other respiratory parameters. The factors facilitating and hindering the improvement of VODRMV under various conditions are considered The great potential benefits from using voluntary optimization of the efficiency of external respiration in hypoxemia induced by strenuous physical exertion or pulmonary disease (bronchial asthma) suggest that it would be desirable to use VODRMV to accelerate human adaptation to decreased partial oxygen pressure in the air breathed. However, this cannot be done without first determining what changes occur in external respiration in various types of adaptation to hypoxia.

These issues are considered in Chapter 4 ("External Respiration and Human Adaptation to Hypoxic Hypoxia"), which begins with a description of the methods for determining human tolerance to acute hypoxic hypoxia. To evaluate adaptation to hypoxia, the authors have developed a complex methodology for determining human tolerance. Their technique includes four provocative tests: 1) determination of "time to unconsciousness" when breathing nitrogen; 2) continuous "ascent" in a barochamber without auxiliary oxygen support at a rate of 20 m/sec. at rest; 3) the same test combined with physical exercise (200 kgm/min.) on a bicycle ergometer; 4) "ascent" in a barochamber without auxiliary oxygen support with 10-minute "plateaus" at altitude equivalents of 5000, 6000, 7000, 8000, 9000, and 10000 m (to the maximum endurable altitude). The first provocative test investigates human tolerance of fulminant hypoxia, the second and third tests measure response to rapidly increasing hypoxia, and the fourth to gradually increasing hypoxic hypoxia. Human tolerance of the combined effects of hypoxia and high or low temperatures has also been studied.

Data are also presented concerning ways to increase human tolerance of acute hypoxic hypoxia: high altitude adaptation, various schedules of barochamber training, fasting, and the use of drugs. It has been demonstrated that human tolerance of acute hypoxia may be improved using high altitude adaptation for as short a period as 7 days, provided training takes place at a sufficiently high altitude. An analogous adaptation-facilitating effect may be obtained even more rapidly using short-term barochamber training. A comparative study of the antihypoxic efficacy of 10- and 3-day "pulsed" schedules of barochamber training showed them to be virtually identical. During testing of three high altitude 3-day schedules of barochamber training (5000, 6000, and 7000 m), it was established that to attain statistically significant increases in human tolerance to acute hypoxic hypoxia "altitudes" must be no less than 6000 m. Human tolerance for acute hypoxic hypoxia can be improved to an extent approximately commensurate with that attained through high altitude adaptation and barochamber training by restricting calory intake for 4 to 14 days. A very rapid increase in human tolerance for gradually increasing hypoxia in a barochamber using single doses of antioxidants has been demonstrated with two drugs — tiguril (the antihypoxic effects of which are associated with rate of oxidative phosphorylation and suppression of free-radical oxidation in tissues) and the psychological stimulant sydnocarb (N-Phenylcarbamoyl-3-(B-phenylisopropyl)-sydnonimine).

Chapter 5 presents data on the state of the external respiration system and human adaptation to acute hypoxia-hypercapnia. The limits of human tolerance to acute hypoxia and hypercapnia have been studied. The observations made by the authors suggest completely satisfactory human endurance for relatively prolonged continuous breathing of a gas mixture containing 16% $CO_2$ and 8% $O_2$. This suggests the possibility that voluntary hypoventilation under conditions of hypoxia may be used tp increase efficiency of external respiration. The possibility of using barochamber training combined with training in voluntary hypoventilation to achieve this effect has been demonstrated. Research on voluntary hypoventilation combined with decreased metabolic rate (achieved through decreased calory intake) is of special interest. It has been

established that through hypoventilation training, one can more than double the duration of slow breathing with nitrogen. Evidently this phenomenon is based on an increase in the respiratory system's sensitivity threshold for hypoxic and hypercapnic stimulation, making it possible to slow oxygen loss with expired air. Improvement of blood supply to the brain and heart at the expense of the peripheral tissues, making use of the characteristics of $pO_2$ dynamics in tissues, is also a possibility.

Thus a logical conclusion of the book is the proposition that through automated optimal decrease in minute volume alone, one can improve utilization of oxygen by the tissues and increase hypoxia tolerance in humans.

The results and largely original theoretical and practical ideas presented in this book suggest new approaches and the prospects of a new research area in physiology -- research on the problem of human adaptation to extreme conditions, especially hypoxia, from the standpoint of the efficiency of external respiration. The work successfully propounds its main idea and is marked by clear and cogent exposition and a specific practical bent.

[Paragraph criticizing specific omissions and inaccuracies in the book omitted]

It would appear that the intention of the authors to evoke interest in the investigation and improvement of methods for voluntary optimization of external respiration, as applied to specific extreme conditions, has been achieved. The monograph develops a number of significant fundamental concepts, and at the same time contains valuable material for physicians, physical education instructors, and specialists in the areas of sports, high altitude physiology, and aerospace medicine, which may be used in practice.

## AVIATION MEDICINE

**PAPERS:**

P1095(24/89)* Lapa VV.
***Information interactions within a "man-flight vehicle" system as a problem in aviation medicine.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 28-32; 1989.
[No references]

Aviation Medicine, Human Performance, Information Processing
Humans, Pilots
Man-Machine System, Flight Vehicles

Abstract: The author argues that the traditional approaches to increasing human resistance to adverse environmental factors and improving work capacity do not provide for optimal performance in flight situations because they neglect the fact that information exchange is the primary mode of interaction within the pilot-flight vehicle system. Such interactions are especially important to aviation medicine in light of the fact that 60% of pilot errors occur in the context of information reception and processing. Information overload or deficit interferes with optimal decision-making and appropriate behavior and constitutes a source of stress, which is in itself detrimental to pilot performance.

This problem was addressed in aviation medicine during the 1950s and 1960s, primarily through attempts to improve information display of indicators and insure that important signals were easy to perceive and interpret. Research in this area tended to reduce pilot performance to the level of mechanical responses to external stimuli. However, analysis of the external environment alone cannot reveal the principles underlying efficient performance; this requires study of psychological processes in the context of the complex cognitive performance requiring support. For example, although common sense suggests that the best flight position indicator would present a view "of the Earth from the aircraft;" when pilots are lost in the clouds, the view "of the aircraft from the Earth" (i.e., a display with a moving aircraft and stationary horizon) has been empirically demonstrated to be preferable since it accords with the pilot's own psychological (as distinct from perceptual) representation of the situation.

The author argues that many aspects of current display systems for flight information may actually be detrimental to pilot performance. There is experimental evidence linking perceptual and cognitive overloading, loss of automaticity in acquired piloting skills, and increased stress to discrepancies between the way flight information is displayed on CRTs and the psychophysical principles determining how the information is transformed into an internal representation. Switching from one information representation system to another (e.g., from CRT to conventional instrument dials) may cause performance to deteriorate and/or consume psychological resources required for decision making. Results obtained in the author's laboratory indicate that if a pilot is to use various information representation systems simultaneously, it is critical that they be psychologically compatible, utilizing identical coding principles and similar display scales for flight parameters. Automated flight decreases pilot activity, which compromises the reliability of his control of system parameters and detriments performance efficiency if an emergency requires resumption of manual control. Measures to increase reliability of pilot performance should compensate for disruption of information interactions. These measures will include optimization of information displays, changes in the form of automated control, and training directed at formation of an optimal internal flight representation. In particular, it may be expedient to retain afferent kinesthetic feedback in automated pilot modes, possibly through use of dual automated/manual control.

Table 1: Quality and structure of pilot actions in response to the need to switch among modes of coding flight parameters

Table 2: Parameters of pilot activity as a function of piloting mode

| Parameter | Piloting Mode | | |
|---|---|---|---|
| | Automated | Dual | Manual |
| **Number of gaze shifts (in 1 min)** | **30-50** | **60-80** | **80-120** |
| Mean EMG amplitude for flexors of the right hand and fingers, μW | - - | .33.6 | 42.7 |
| Probability of recognizing autopilot failure | 0.36 | 1.0 | — |
| Probability of timely correction of results of autopilot failure | 0.5 | 0.9 | — |

Figure: Characteristics of pilot performance in an emergency as a function of information provided to support recognition and decision-making

P1118(24/89)* Dlusskaya IG, Kiselev RK.
***Certain applied aspects of biochemical research in aviation medicine.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 15-21; 1989.
[76 references; 43 in English]

Aviation Medicine, Biochemical Parameters, Endocrinology, Metabolism
Humans, Pilots
Psychology, Stress; Human Performance, Flight Performance,

Abstract: This paper reviews data on biochemical studies of flight crews. During the period 1955-65, many studies were guided by the theories of G. Selye on the general-adaption syndrome and the role of hormones of the adrenal cortex. This work showed that during short-term flights and the 1.5-2 hours subsequent to them, there is a moderate increase in cholesterol, urea, and ammonia in blood. At the same time there is enhanced renal excretion of urea, uric acid, creatinine, urokinase, and $K^+$, $Na^+$, and $Mg^{++}$ ions. These results were believed to demonstrate a catabolic effect and disruption of protein resynthesis under stressful flight conditions. Other data demonstrated increased hydroxyketosteroids in blood and saliva and increased renal excretion of the same substances. Subsequent to this period, the effects of long-term (20-50 hours) flight and prolonged simulated combat exercises were studied. Results included increased excretion of adrenalin and noradrenalin, altered diurnal rhythms in excretion of corticosteroids and catecholamines, involving decreases in diurnal and increases in nocturnal excretion. In some cases exhaustion of the adrenal cortex resulting from too much stress was suspected. Most studies showed marked correlations between magnitude of corticosteroid, catecholamine, and metabolic responses and complexity or difficulty of flight performance. It was found that in experienced pilots biochemical stress response was inversely proportional to quality of flight performance. A number of biochemical indicators were combined in some works to produce a "stress index." Mathematical processing of data on rate of recovery of physiological and biochemical processes was used to construct a recovery curve and thus prescribe the minimum rest period after a flight of a given duration.

Another set of studies, performed primarily in Italy, prescribed countermeasures for flight-induced changes in metabolism. These included drugs that optimize liver function, provide high energy, improve metabolism in brain tissue and compensate for dysfunction in the adrenal cortex. Soviet studies recommended the addition of multivitamins to the diet. Such supplements led to a decrease in illness rate in flight crews.

Studies addressing hormonal and metabolic status before take-off are also of interest. Responses are much less extreme in experienced pilots and such responses can be "extinguished" through training. On the other hand, pre-take-off stress is also a sign of readiness for a difficult or dangerous flight. Attempts to predict flight performance from such indicators have had the following results: 1) individuals with very high professional qualifications and fewer accidents show an adrenalin, but not noradrenalin type reaction before take-off; 2) a moderate degree of activation is associated with higher accuracy in job performance, but an extreme response is associated with performance deterioration.

Biochemical indicators have also been used to attempt to predict susceptibility to hypertension and ischemic heart disease, both very common in flight crews. Risk factors for these diseases in young flight crewmembers include increased extracellular Na in lymphocytes, and increased glucose, cholesterol, and uric acid in blood. Methods for early diagnosis of hyperlipedemia using ratios among different types of lipids, and changes in blood cholesterol and triglycerides with age are being developed for Soviet flight crews. The countermeasures that have been developed have decreased cholesterol by 11% and triglycerides by 44.5% in at-risk crewmembers

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

**PAPERS:**

P1097(24/89) Silenko OV.
***The reactions of the cardiovascular system to static loading when body position is changed.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 34-38; 1989.
[17 references; 8 in English]

Cardiovascular and Respiratory Systems; Cardiovascular Response
Humans, Males
Static Loading, Body Position, Upright, Head-Down

Abstract: Studies were performed on 19 healthy males, aged 24 to 41. Subjects were placed on a tilt table in a sitting position. A static loading task was assigned involving using the legs to maintain pressure on a device consisting of two panels separated by a pneumatic chamber. Subjects performed the test in horizontal, head-down (-10°) and upright positions (40°) at 1-week intervals. Static loading was 30% of the individual's maximum and averaged 360 W. Physiological measurments were recorded at minutes 18 and 20 in each of the three positions at rest, at minutes 1, 3, 5, 7, 9, and 12 of loading test, and during minutes 1 and 5 of the recovery period. These included: an EKG from a single lead; a tachyoscillogram of the brachial artery; a venous/arterial pulsogram of the vascular fascicle of the neck and the area of the shoulder, with pressure in the occlusion cuff gradually increasing from 0 to 400 mm Hg; an ultrasound Doppler cardiogram from the area of the fifth intercostal space to the left, at the edge of the sternum; and a tetrapolar impedance plethysmogram of the chest. The following parameters were measured: heart rate; diastolic, mean dynamic, true systolic, and end systolic blood pressure; blood pressure in the jugular vein and brachial veins; stroke volume and cardiac minute volume; contraction strength and energy expenditure of the left cardiac ventricle; pattern of stroke and minute volumes of effective coronary blood flow; amplitude and rate of shifts of cardiac elements during systole and diastole; specific actual peripheral resistance; difference between this and specific working peripheral resistance, change in the oscillatory index of the brachial artery; amplitude of initial and dicrotic pulsation of brachial arterioles and small arteries.

The majority of subjects rated task performance to be more difficult in the head-down and upright positions. Cardiovascular response to loading occurred quickly. In all positions heart rate increased, starting at minute 1. Increases were greatest in upright and least in horizontal position. All blood pressure parameters increased in response to static loading. Significant differences in blood pressure response to loading in different positions were noted in diastolic and end systolic pressure. The former was lower in horizontal position than in upright position in minute 3 and higher in minutes 1, 5, and 9. The same parameter was higher in upright than head-down position in minutes 3, 5, and 7 and during recovery. End systolic pressure was highest in upright position. The increase of the oscillatory index of the brachial artery in response to static loading was greatest in upright and least in horizontal position. Specific actual peripheral resistance increased only moderately in response to loading in all positions and did not increase as static loading did. Before loading, the difference between actual and working peripheral resistance in upright position was 145% higher than in horizontal and 45% higher than in head-down position. The corresponding figures for minute 1 of loading were 45% and 14%. Starting at minute 2, the differences increased to 53-62% in upright and 22-24% in head-down position. Thus, resistance to blood flow in upright position decreased by a factor of 2.5 in upright and 2 in head-down position. Although data on minute volume seem to suggest that venous return of blood to the heart was comparable (moderate increase) regardless of body position, changes in pressure in the jugular vein presented a different picture,

decreasing by 33% in horizontal, 23% in head-down and 15% in upright position. The authors argue that the response to static loading limits increases in blood pressure. In horizontal position this response occurs primarily through pooling of venous blood and decrease in its return to the heart. In upright position the same effect is achieved by decreasing tonus of arteries and arterioles. In head-down position both mechanisms occur equally. The decrease in venous pressure after static loading also serves to increase perfused pressure in the vessels of the head without involving arterial blood pressure, which otherwise would also increase. Results indicated an increase in parameters related to increased loading of the heart. Strength of contraction increased by 29-35% in horizontal position, by 19-24% in head-down, and 36-45% in upright position, In minute 12 of loading, minute volume of coronary blood flow increased 49% in horizontal, 67% in head-down and 100% in upright position. Data are interpreted as suggesting that static loading has a stronger effect on the cardiovascular system in upright position, and is stronger in head-down than in horizontal position.

Table: Change in parameters of circulation in response to static loading in various body positions

P1100(24/89) Gansburgskiy AN, Potapov PP, Altukhova VV, Degtyareva MA.
***Morphometric analysis of the aortal endothelium and serum lipoproteins in rats during the period of readaptation after 15 days of hypokinesia.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 46-49; 1989.
[13 references; 1 in English]
Cardiovascular and Respiratory Systems, Morphology, Aortal Endothelium, Metabolism, Lipoproteins
Rats
Hypokinesia

Abstract: Experiments were performed on 40 white rats, 34 of which were housed in immobilization cages. At the end of 15 days of hypokinesia the animals were transferred to common cages; seven were sacrificed on day 15 of treatment and one each day during the subsequent 27 day recovery period. The aorta was isolated in the sacrificed animals, fixed and the endothelium prepared and stained. An ocular micrometer was used to measure the mean areas of endotheliocytes, their nuclei and cytoplasm, and the nucleus-to-plasma ratio was computed. Morphometric analysis was performed on 375-450 cells. In addition, the numbers of endothelial cells displaying karyopyknosis, karyolysis, and double nuclei were computed for 8000-10000 cells per subject. Numbers of lymphocytes and monocytes in the endothelial layer were estimated. Additionally, elongation of cells and changes in the form of their nuclei were noted as signs of migration of lymphocytes and monocytes through the layer. Lipoproteins were isolated in serum by disc-electrophoresis in a polyacrilamide gel. The dynamics of each parameter were recorded. The Wilcoxon-Mann-Whitney test was used to determine statistical significance.

On day 15 of hypokinesia the quantity of serum β-lipoproteins and pre-β-lipoproteins increased, while concentration of α-lipoproteins decreased. This change can be considered atherogenic. Concentration of β-lipoproteins were below control from days 19-23 of readaptation, but fluctuated during the last 10 days of the experiment. During the recovery period signs of destructive processes in the endotheliocytes were retained. Although the number of pyknotic nuclei decreased compared to their level during hypokinesia, they remained above the norm. Karyolytic nuclei were also elevated, peaking at the end of week 3 of recovery. During the readaptation period, the quantity of lymphocytes and monocytes in the endothelial layer increased. All these changes can be considered destructive. However, after 2 weeks of recovery, an increase in the number of binucleate cells was observed, suggesting stimulation of regenerative processes. These processes evidently could not fully compensate for destruction, since beginning on day 12 of readaptation there were signs of lack of correspondence between the number of endotheliocytes and the area they occupied (increased area of cells and cytoplasm). Area of nuclei also increased, but growth was slower and less pronounced than increased cell area, leading to a marked decrease in nucleus: plasma ratios on days 14-19 of recovery. While changes in endothelial structure were less pronounced during recovery than during treatment, it should be noted that complete recovery had not occurred even 27 days after treatment termination.

Figure 1: Changes in the fractional composition of serum lipoproteins in rats during readaptation after 15 days of hypokinesia

Figure 2: Changes in the relative concentration of various cell forms in the endothelial layer of rat aortas during readaptation after 15 days of hypokinesia

Figure 3: Changes in the stereological parameters reflecting the state of the aortal endothelium of rats during readaptation after 15 days of hypokinesia

P1107(24/89) Baranov BVS, Yakhontov BO.
***Recording of intrathoracic pressure in animal experiments.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 71-73; 1989.
[6 references; 1 in English]

Cardiovascular and Respiratory Systems, Intrathoracic Pressure
Animals, Small
Equipment and Instrumentation, Tensometric Sensors, Implanted

Abstract: The usual method for studying intrathoracic pressure in animal experiments utilizes an esophageal probe, the recommended instrument for humans. However, this probe irritates the animal's throat, disrupts its behavior, and cannot efficiently be used on small animals. The authors recommend implanting miniature tensometric pressure sensors in the pleural sinus, resting on the diaphragm with the sensitive membrane facing the lung. The animals have been found to recover from this type of implantation operation within 2-3 days.

Figure 1: External appearance and design of the implanted pressure sensor

Figure 2: Diagram of the implantation of an intrathoracic pressure sensor

Figure 3: System of calibration of the implanted pressure sensor and sample of the recording of an intrathoracic pressure curve with calibrated signal

P1119(24/89)* Dronenko SV.
***Orthostatic tolerance of athletes in different sports and changes in it in response to hypogravity.***
Voyenno-Meditsinskiy Zhurnal.
1989(5): 62.
[No references]

Cardiovascular and Respiratory Systems, Orthostatic Tolerance
Humans, Athletes, Nonathletes
Hypogravity, Immersion

Abstract: Orthostatic tolerance was evaluated in athletes before and after exposure to hypogravity created through the dry immersion model. A total of 60 subjects participated, males aged 21-39. Subjects were divided in three groups. Group 1 (n=7) contained gymnasts; group II contained participants in the decathlon; group III contained basketball players (n=10); group IV rowers (n=8); and group V contained 26 healthy individuals who did not participate in sports. The dry immersion treatment lasted 3 days.

A tilt test (to angle +70° for 20 minutes) was performed before and after treatment to determine orthostatic tolerance. The following parameters were measured during the test at minutes 1, 5, 10, 15, and 20 and in minutes 1, 5, and 10 of the recovery period: stroke volume, pulsed blood flow in the thigh and calf (through impedance plethysmography), heart rate, systolic and diastolic blood pressure, cardiac minute volume, total peripheral resistance, pulsed and mean dynamic blood pressure.

In the baseline period, subjects in groups III (basketball players) and I (gymnasts) displayed especially high orthostatic tolerance compared to other athletes. However, only basketball players showed greater endurance for the test than nonathletes. Immersion decreased orthostatic tolerance in all subjects. The smallest change was noted in gymnasts and nonathletes. The author relates the decreased tolerance to orthostatic effects in athletes to their diminished capacity for adaptation of the blood pressure regulation system. After immersion, systolic blood pressure fluctuated from 123 to 103 mm Hg in rowers, while it only fluctuated by 8 mm Hg in nonathletes. Peripheral resistance during the test after immersion was only adequate (increased by 40-50%) in basketball players and gymnasts.

P1110(24/89) Modin AYu.
***Analysis of the information provided by amplitudinal and temporal characteristics of the early diastolic complex of a differential thoracic impedance plethysmogram***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 79-80 1989.
[4 references; 1 in English]

Cardiovascular and Respiratory System, Early Diastolic Complex; Impedance Plethysmography, Thorax
Humans, Males
Tilt Tests, Immersion,

Abstract: The objective of this work was to determine whether the parameters of diastolic/systolic coefficient and duration of isometric relaxation phase on a differential thoracic impedance plethysmogram can be used as an indirect assessment of physiological fluctuations in the left ventricle filling pressure in healthy individuals. Subjects in the experiment were 26 apparently healthy male volunteers. Each subject was given a differential thoracic impedance plethysmogram using tetrapolar leads. Parameters were recorded in passive upright (+70°) and head-down (-15°) positions (tilt tests). Subjects also underwent dry immersion. The records were used to compute the diastolic/systolic coefficient (DSC), (ratio of diastolic wave amplitude to systolic wave amplitude) and duration of the isometric relaxation phase (IRP) was measured as the time from the peak of the "P" wave on an EKG to the peak of the "R" portion in the "QRS" complex. Differences were tested statistically with a paired t-test.

Passive assumption of upright position was associated with a reliable decrease in DSC averaging 31%, but no change in IRP. Head-down position and immersion were associated with significant increases in DSC, 16 and 13%, respectively. No significant changes were observed in IRP. The authors conclude that DSC can serve as an indirect indicator of end systolic pressure in healthy individuals. The functions relating these two parameters may differ in healthy people and those with ischemic heart disease.

Table: Amplitude and temporal characteristics of a differential thoracic impedance plethysmogram in response to different positions

## DEVELOPMENTAL BIOLOGY

**PAPER:**

P1092(24/89) Serova LV.
***Adaptive capacities of the mother-fetus system under conditions of weightlessness.***
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 1139-147.

Developmental Biology, Reproductive Biology, Adaptation
Rats, Neonates, Fetuses, Pregnant Females; Males
Space Flight, COSMOS-1514, COSMOS-1667

Abstract: The results of the embryological experiment on the COSMOS-1514 biosatellite demonstrate that pregnant mammals (Wistar line rats) adapt to space flight and mobilize the reserves essential for development of the fetus. The flight was relatively short in duration, 5 days, but it occupied slightly less than 1/4 of the total gestation period of rats. The animals spent days 13 to 18 of gestation in space. This is the period of active fetal growth and formation of the nervous and endocrine systems, the skeleton, muscles and visceral organs. The organisms exposed to weightlessness on the whole developed successfully under space flight conditions. During space flight the rat fetuses continued to grow and develop, lagging behind control animals only slightly; they completed their development after return to Earth -- during the period of readaptation of the maternal organism to normal gravity. Each animal reached sexual maturity and, in turn, produced offspring.

Exposure to weightlessness from days 13 to 18 of pregnancy induced a broad range of changes in the mother's body, most of which were relatively serious. An overall indicator of these changes was the fact that the body weight of the female rats exposed to flight was 60 g, (virtually one quarter of the rat's total weight) lower than that of the control animals. Similar lag in weight gain can be produced in pregnant rats by feeding them 50% of their normal diet. In the space flight experiment, the animals of the flight group consumed approximately the same average amount of food (100% of the normal diet) as the controls. Thus, the lag in weight gain can be attributed to activated catabolic processes during flight.

In an experiment on biosatellite COSMOS-1667, male rats exposed to weightlessness for 7 days did not show a similar decrease in weight gain compared with animals in a vivarium control group (Table 46).

The effects of space flight factors on a number of other parameters were more severe in pregnant females than in males. Thus the females showed substantial leukocytosis, while the males displayed no changes in leukocytes concentrations postflight (cf. Table 46); at the same time, the lymphocyte:neutrophil ratio was analogously decreased in both cases. The females displayed a decrease of 24% in hemoglobin concentration ($p<0/001$) compared to the controls, while in the males the concentration of hemoglobin tended to be elevated in the flight group.

The extent of thymus involution (-30%) was greater in pregnant female rats exposed to weightlessness than in males (-15%).

Given such significant changes in the mother's body, one might expect rather serious changes in the major indicators of reproductive functions and viability of the offspring. Because this was the first experiment on mammalion ontogeny in space and was exploratory in nature, the period of prenatal exposure was selected to minimize likelihood of fetal death and maximize the number

of animals available for postflight studies. In addition, attempts were made to keep the adverse side effects associated with launch and reentry factors to a minimum.

In the last third of pregnancy the mother-fetus system is most resistant to harmful factors. During this period, even severe bleeding or food deprivation has little effect on fetal development. However, S. M. Barlow subjected rats to immobilization stress at various stages of pregnancy — from days 9 to 20 — and found that changes attributable to treatment during the latter portion of pregnancy were not only as great, but for a number of parameters even greater than after immobilization during early stages of pregnancy. Other studies have also found behavioral responses of offspring to be affected by treatment of mothers during this period.

Based on these data, one might expect the period of pregnancy (days 13-18) selected for exposure to weightlessness, while not critical with respect to general fetal viability, to be critical for individual organs of fetuses developing in space. Changes in the rate of development of individual components of complex functional systems might have been expected and this might have affected the establishment of motor reactions, development of sensory systems, and behavior

The flight experiment was designed to maximize detection of any disruption of the developmental process during various stages of postnatal life up to the development of sexual maturity.

However, the data obtained establish the fact that it is possible in principle for mammalian fetuses to develop normally when the mother is exposed to weightlessness and other space flight factors during pregnancy. However, observation of animals during various stages of development revealed a number of differences between the flight animals and control rats. These differences are discussed below.

On the day of reentry -- day 18 of pregnancy -- the experimental group showed signs of delayed develop compared to the controls, as evidenced by diminished weight gain, greater concentration of fluid in the tissues, and retarded development of ossification sites in various portions of the skeleton. The differences between the experimental and control animals were small for all parameters (within 10%), but were statistically reliable. They could have resulted from a decrease of placenta size and changes in its structure in the experimental group.

It is interesting to consider that similar changes were observed in fetuses developing while the mothers were exposed to hypergravity of 2 g during pregnancy. In this situation the experimental fetuses also lagged behind the controls in body weight and size of ossification sites; and the changes were virtually identical in magnitude to those occurring in fetuses that developed in zero-g.

Retardation of growth and development is a universal reaction of the fetus when the mother is exposed to a variety of adverse factors For this reason the presence of such changes in animals that develop in weightlessness was not unexpected. More unexpected was the relatively mild and rapidly reversible nature of these changes. Thus, neonate rats born 5 days after their mother's return to Earth did not have lower body weight than animals of the synchronous control, and were even ahead of animals of both control groups with respect to size of ossification sites.

The next difference between the experimental and control groups was the longer and more difficult labor of female flight rats. Of five experimental animals allowed to give birth at natural term, only two gave birth without complications and at the normal time. In one flight rat, labor lasted 2 days, which, aside from exhaustion and muscle weakness of the mother, was due to the presence of an oversized fetus. Because delivery of this fetus, which was first in the birth canal, was slow, delivery of the remaining fetuses was delayed. The remaining fetuses, full-term and fully developed, died of anoxia because of the long interval between the

detachment of the placenta and their delivery. It should be noted that no analogous cases could be found for normal, full-term litters, in the births of no fewer than 1000 animals born in other experiments.

Two other animals of the flight group also had prolonged labor, although in both cases the delivery was less prolonged and difficult than the case described above. Each of their litters contained one dead neonate.

Similar complications of the birth process have been observed in animals anesthetized continuously for 2 days before and during labor and in animals adrenalectomized before or during pregnancy.

It should be emphasized that the major differences between the experimental and control groups observed during this stage of the experiment were associated with labor difficulties and not with characteristics of fetal development in weightlessness or during readaptation.

During the initial days of postnatal life, an additional significant difference between the experimental and control group became evident, namely the increase in death rate of the neonates developing in weightlessness. Cases of neonate death were not observed in all experimental litters, but only in litters of the females having prolonged, difficult labor, which may have been the reason for the weakness and death of a portion of the neonates.

The increase in the death rate of neonates during the early postnatal period could also be a result of the disruption of maternal behavior in the flight mothers, which is very widespread in experiments involving stress during pregnancy. However, observations of the nursing animals and quantitative recording of components of maternal behavior revealed no substantial differences between groups. This observation appears especially interesting in light of the serious changes occurring in the mother's body during flight and subsequent labor. Animals exposed to space flight factors were able to sustain fetal development, providing the essential homeostasis, and to maintain normal maternal behavior during lactation.

When the juvenile rats were examined in the first month of postnatal life, an extensive research program was conducted to assess growth rate and general development, physiological endurance, development of motor skills and coordination, and the pattern of development of the sensory systems. In the majority of parameters the experimental animals did not differ from the controls. Indeed, it is surprising that, given the serious changes in the mothers' bodies induced by weightlessness, the maturation process and initial functioning of the sensory systems occurred on schedule, and that formation of the central nervous system and its interactions with other systems were normal.

Despite the indubitable "success" of the young rats from the flight group, certain differences from the control group observed during this stage of the research should be noted. Thus, the animals' vestibular function was tested on a rotating platform on day 2 of their lives, the number of rats that unambiguously demonstrated the reflex of turning their head opposite to the direction of rotatio was 20% higher in the flight than in the control groups. On day 14 of life, 65% of the flight rats had opened their eyes, compared to 37% of the control rats. At the same time, the flight rats showed delays in hearing development compared to control animals. In all cases, the differences between experimental and control groups were small and rapidly disappeared during subsequent development without seriously affecting the overall schedule of growth and development. They cannot be considered signs of developmental delay, because experimental animals were ahead in some parameters, while lagging behind in others. Rather a degree of developmental "instability" could be deduced in the animals spending a portion of the prenatal period in weightlessness. This "instability" is manifest in other parameters. In rate of growth, the flight group were ahead of the synchronous control group, but behind the

vivarium control group — with no differences statistically significant. However, the variance in weight of the flight rats was greater than in the controls. The "instability" of the blood system in the flight animals, as manifested by fluctuations in concentrations of hemoglobin and number of hemopoietic stem cells at certain measurement points during the first month of life, is also worthy of note.

When motor activity and motor coordination were studied in the rats during the first weeks of their lives, no significant differences were found between the experimental and control groups, with the exception of a slight decrease in static endurance, as indicated by the amount of time the animals could hold onto a cross bar on days 15 and 18 of life. Study of metabolism and contractile capacity of skeletal muscles when some animals were dissected on days 15, 30, and 100 of life also failed to reveal significant differences among the experimental and control animals.

One of the most sensitive criteria for evaluating the mother's capability to maintain homeostasis for the developing fetus is the state of its brain, especially the more complex cortical areas. Status of these structures was assessed at various stages of postnatal ontogenesis by testing the animals with learning and behavioral tests varying in complexity. A reliable difference was found among the experimental flight rats in the "open field," manifesting itself in decreased total length of the path traversed by the experimental animals, fewer orienting reflexes, and fewer visits to the center of the field. Intergroup differences in these parameters were observed on days 30 and 51-53 and had disappeared by the time the animals were 3 months old.

The offspring of flight and control rats displayed virtually identical capacity to learn mazes varying in complexity. However, when tested on a Dombrovskiy maze, the experimental group showed higher levels of goral-irrelevant behaviors. (significant increase in grooming time and in number of secondary movements). Analysis of the results suggested that these changes were associated with attenuation of neural inhibition and less focus to the excitatory response. The changes observed in the experimental group were not gross: the animals oriented themselves normally to their new surroundings, were able to master the relatively complex tasks, adapted their experience to a changing situation, and tolerated significant levels of functional stress.

When animals spending a portion of their prenatal development time in space were dissected on days 15, 30, and 100 of their lifes, no differences were betweem control and experimental groups in the weight of visceral organs, metabolism of fluid, electrolytes, fats, nucleic acids, or biologically active substances. In other words, exposure to weightlessness during the fetal period, at the stage during which visceral organs and the mechanisms regulating their functioning are formed, did not affect the rate of growth of the organs or the level of metabolism in them at various stages of postnatal life up to the attainment of sexual maturity.

The single difference between the experimental and control group that was revealed in this portion of the research, was the alteration of collagen metabolism in bone tissue and skin of the animals developing in weightlessness, attesting to a certain delay in development of connective tissue. The reasons for these changes are still unclear. The presence of similar changes in skin and bone tissue suggests the effects are systemic in nature. Regulation of biosynthesis and catabolism of the organic component of connective tissue is complex, with an important role played by hormones. It may be hypothesized that the cause of the changes in collagen metabolism observed during the postflight period in the animals developing in weightlessness, is the change in the hormonal status of the mother rats during the flight. It is true that the postflight examination of the rats did not reveal significant changes in hormone concentrations in blood plasma; however, the changes noted in the target organs (involution of the thymus, neutrophilia and lymphopenia), as well as the significant delay in increases in body weight suggest that during the flight, the hormonal status of the mothers' bodies was significantly altered.

It should also be noted that when the juvenile rats were examined at various stages of postnatal ontogeny, no differences were observed between the experimental and control groups in body and organ weight, hormonal status, weight of lymphoid organs, or leukograms of peripheral blood, while at the same time intergroup differences in collagen metabolism in skin and bone tissue existed at every examination point.

These results support a relatively high evaluation of the adaptive capacities of the mother-fetus system in response to exposure to weightlessness during the last third of pregnancy. Space flight conditions were not unimportant to the mother's body and required significant mobilization of compensatory mechanisms. This mobilization was quite effective: the mothers succeeded in supporting normal homeostasis in the fetuses and in providing them with materials for anabolic metabolism. The retardation of fetal development during flight was very slight and was recovered rapidly during subsequent development. Changes in the mothers' bodies occurring during flight were also functional and reversible: beginning on the first day after reentry, the female rats of the flight group started to gain weight rapidly. After delivery, they maintained normal maternal behavior during the lactation period and supplied their offspring with sufficient milk.

The juvenile rats that spent part of the prenatal development period in weightlessness, proceeded through the entire sequence of postnatal development, up to sexual maturity and reproduction. The differences between the experimental and control animals detected at various stages of the research were small and disappeared rapidly. They should not be considered defects or changes in developmental rate.

The most serious changes observed in the animals of the flight group were the complications of the birth process. The difficult, prolonged labor of the mothers was the apparent cause of the serious differences between neonates of the flight and control groups: death of some neonates during labor, increased death rate in the early postnatal period of animals that developed during weightlessness and even later, offspring of these neonates had higher deathrates.

When the data obtained are analyzed, significant within group individual differences can be noted in the flight animals. The differences were especially clear when the females began to give birth. When dissected on day 18 of pregnancy, the mothers exhibited no essential differences in reproductive function or state of the fetuses. Yet, during delivery animals in the same group manifested large differences.

Significant individual differences in reactions to weightlessness have also been observed previously in male rats flown on COSMOS biosatellites; and findings in animals exposed to hypergravity have been analogous.. The reason for the large individual differences observed in animals exposed to weightlessness and hypergravity proabably can be attributed to the fact that "conditions of stress differentiate the population with respect to the reactions of its members to the stress factor." The experimental data obtained demonstrate the fact that normal fetal development of mammals can in principle take place when the mother is exposed to weightlessness during pregnancy, although rather serious changes (including death of offspring) are also possible in individuals. This should not be ignored, because individual differences in resistance and reactivity are a universal characteristic of animals, and, as environmental conditions change, these form the basis for natural selection and evolutionary development .

Table 46: Body weight and blood profile of male rats after 7-day flight on COMSOS-1667

| Group | Body wt, g | Hemoglobin, g% | Leukocytes, thous./mm$^3$ | Lymphocytes, thous./mm$^3$ | Neutrophils with segmented nuclei, thous./mm$^3$ | Lymphocytes / Neutrophils |
|---|---|---|---|---|---|---|
| F n=7 | 332±3 | 15.4±0.2 pv<0.01 | 8.1±0.5 | 2.6±0.2 pv<0.001 ps<0.002 | 5.3±0.4 pv<0.002 ps<0.001 | 0.52±0.05 pv,s<0.01 |
| SC n=7 | 349±5 | 14.5±0.3 | 10.2±0.8 | 7.0±1.0 | 3.0±0.3 | 2.7±0.7 |
| VC n=7 | 334±6 | 14.13±0.3 | 8.6±1.0 | 7.5±0.7 | 2.14±0.6 | 3.16±0.7 |

## ENDOCRINOLOGY

**PAPERS:**

P1109(24/89) Afonin BV.
***The effect of space flights and hypokinesia with head-down tilt varying in duration on concentration of insulin in the blood.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 77-79 1989.
[17 references; 4 in English]

Endocrinology, Insulin
Humans, Cosmonauts
Space Flight, Long- and Short-term, Soyuz, Salyut-7, Hypokinesia With Head-Down Tilt

Abstract: The objective of this work was to compare changes in blood insulin levels after completion of long- and short-term space flights and also after exposure to hypokinesia with head down-tilt. Subjects were 16 cosmonauts completing short-term (5-8 days) space flight on Soyuz, 15 cosmonauts in long-term (120-240 days) flight on Salyut-7, 10 volunteers undergoing short-term hypokinesia with head-down tilt (-10°) lasting 7 days, and 6 volunteers subjected to 120 days of hypokinesia with head-down tilt (-15°). Insulin concentrations were measured in serum from venous blood, taken in the morning on an empty stomach. Concentrations were measured in the cosmonauts: 30 days preflight and 1 day postflight; in 7-day hypokinesia subjects: before treatment on day 6 of treatment, and on day 1 after its termination; in 120-day hypokinesia subjects: 30 and 7 days pretreatment, on days 27, 56, and 96 during treatment and on day 1 of the recovery period. Insulin was measured using radioimmunoassay. Results were tested using Student's t.

Immediately after short-term flights, cosmonauts displayed elevated levels of insulin compared to preflight levels. If insulin elevation is a consequence of response to stress during the acute period of readaptation, it should be even more elevated after longer flights. However, on day 1 of readaptation after long-term flights, insulin concentrations, although elevated were no more so than after short-term flights.

On day 1 after 7 days of hypokinesia, insulin concentrations were elevated to approximately the level recorded after short-term flights. Insulin concentrations were also high on day 6 of head-down treatment. By analogy, this result suggests that for short-term flights postflight elevation of insulin is a consequence of its elevation inflight. After long-term hypokinesia, insulin was elevated to approximately the same extent as after short-term treatment. This effect was preceded by increased insulin concentration during the last half of the 120-day hypokinesia period.

The author concludes that after completion of long- and short-term space flights, insulin levels increase in blood to an extent similar to that after hypokinesia with head-down tilt comparable in duration. Increased insulin concentration during the acute period of readaptation can be hypothesized to have been preceded by changes in insulin during space flight. These changes may be hypothesized to be similar to those occurring in long-term hypokinesia with increased insulin during the first month of treatment, normalization during month 2, followed by a stable elevation, retained on day 1 of recovery.

Table 1: Concentration of insulin in blood (in μunits/ml) during 7-day hypokinesia with head-down tilt (-10°)

| Parameter | Norm | Baseline | Hypokinesia, Day 6 | Recovery |
|---|---|---|---|---|
| Insulin | 2-22 | 12.1±1.8 | 17.3±3.2 | 20.3±3.2 |
| *p* | | | < 0.05 | < 0.05 |

Table 2: Concentration of insulin in blood (in μUnits/ml) in response to 120-day hypokinesia with head-down tilt (-5°)

| Parameter | Baseline | Hypokinesia, day | | | | Recovery |
|---|---|---|---|---|---|---|
| | | 2 8 | 5 6 | 7 0 | 9 7 | |
| Insulin | 9.9±1.0 | 21.0±3.5 | 13.4±2.7 | 23.6±3.9 | 16.2±2.1 | 19.5±3.4 |
| n | 12 | 6 | 6 | 6 | 6 | 6 |
| *p* | | < 0.05 | | < 0.05 | | <0.05 |

Table 3: Concentration of insulin in blood (in μUnits/ml) in cosmonauts completing long- and short-term flights

| Parameter | Short-term flight | | Long-term flight | |
|---|---|---|---|---|
| | Pre | Post | Pre | Post |
| Insulin | 6.9±1.3 | 16.4±2.6 | 8.4±1.0 | 15.8±2.3 |
| p | — | < 0.01 | — | <0.05 |
| n | 16 | 16 | 15 | 15 |

P1114(24/89)* Vorob'yev DV, Petrichenko IYe.
***The effect of long-term hypokinesia with head-down tilt on tissue sensitivity to glucocorticoids.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 85-86; 1989.
[17 references; 4 in English]

Endocrinology, Glucocorticoids, Tissue Sensitivity
Humans, Males
Hypokinesia with Head-Down Tilt; Countermeasures, Drugs, Exercise

Abstract: Research was performed on 10 healthy male volunteers aged 29 to 42, divided into 2 groups. In group A a set of pharmacological countermeasures and physical exercises was used starting on day 21 of a period of hypokinesia with head-down tilt, apparently lasting 196 days. In group B, physical exercise was started on day 121. Venous blood was taken on an empty stomach in a baseline period and on days 28, 68, and 196 of hypokinesia with head-down tilt. Lymphocytes were isolated and washed with a phosphate buffer, diluted in medium 199, and divided into equal portions. $^{3}$H-dexamethasone (1 nM) was added to all samples and unlabelled dexamethasone was added to one of the dilutions. A thousandfold excess of unmarked hormone was used for determining nonspecific binding. The samples were incubated for 12-16 hours at 24°C. Then the lymphocytes were washed twice with chilled phosphate buffer and broken down in a 95% solution of ethanol. After bound radioactivity was measured the number of binding sites (receptors) per cell was determined and a constant of dissociation of cytosol glucocorticoid receptors to dexamethasone was computed. The concentrations of ACTH and hydrocortisone were also measured in plasma samples taken on an empty stomach during the baseline period and on days 69 and 196 of hypokinesia. The results were statistically tested using Student's t.

In the baseline period, parameters were within normal limits and no intergroup differences were noted. No correlations were found between concentration of hydrocortisone and number of receptors, or between hydrocortisone concentration and constant of dissociation. On day 28 of hypokinesia, number of glucocorticoid receptors had increased in all subjects by a factor of 1.5-2 and constant of dissociation had increased, suggesting a decreased receptor affinity for the hormone. On day 68, the number of receptors had decreased, to a greater extent in group A. The dissociation constant had decreased in both groups somewhat, but remained above baseline. By day 196 of hypokinesia number of glucocorticoid receptors had returned to baseline in group A, and remained only slightly above it in group B, while the dissociation constant was below baseline in both groups, suggesting increased affinity of the receptors to the hormone. ACTH in blood was elevated on day 68 of hypokinesia, but had decreased significantly by day 196, although remaining above baseline.

This study is interpreted as indicating that during long-term hypokinesia, sensitivity to glucocorticoids changes cyclically with alternating periods of elevation and depression. The period of sensitivity coincided with elevation of ACTH in the blood. Such changes suggest the development of adaptive process in the pituitary-adrenal cortex system, the target organs, under conditions of long-term hypokinesia.

Table: Characteristics of glucocorticoid receptors of lymphocytes and concentration of ACTH and hydrocortisone in blood in subjects of two groups during long-term hypokinesia with head-down tilt

**PAPERS:**

P1105(24/89) Bragin LKh.
***Pattern of changes in acid-base equilibrium of human blood in response to prolonged exposure to an atmosphere containing acetic acid fumes.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 65-68; 1989.
[19 references; 3 in English]

Hematology, Acid-Base Equilibrium
Humans
Habitability and Environment Effects, Airtight Environments, Acetic Acid Fumes

Abstract: Two 20-day experiments were performed utilizing eight apparently healthy subjects, aged 25-44. The purpose of the experiments was to identify the effects of two different concentrations of acetic acid fumes on blood acid-base equilibrium. Fume concentration in the atmosphere of an airtight environment was 15 mg/m$^3$ from days 3 to 20 in Experiment 1 and 25 mg/m$^3$ from days 11 to 20 in experiment 2. Concentrations were selected to provide information about the threshold for effects of this substance. Analogous studies with concentrations of 5 and 10 mg/m$^3$ of acetic acid fumes had no effects on acid-base balance, blood gases or parameters of external respiration. Air temperature was raised to 33° in both experiments on days 16 to 19, and in experiment 2 from days 6 to 9 as well. Subjects ate a standard diet. Arterialized capillary blood was taken from seated fasting subjects in a state of relative rest. A total of 52 samples were studied, including 20 in the baseline and recovery periods.

In experiment 1, plasma $CO_2$, metabolic pH, and actual and standard bicarbonate were elevated on day 6, while blood oxygen was depressed. By day 13 these parameters had normalized. The 3-day period of elevated temperature had no effect on parameters. In experiment 2 at the end of the first 3-day period of elevated temperature (before acetic acid fumes were introduced) oxygen pressure in alveolar area decreased. At the end of the second temperature elevation (in the presence of acetic acid fumes), there was a reliable shift in the parameter of base equivalence, an indicator of compensation for extra $CO_2$ buffers in the blood system. On day 7 of recovery parameters of $pH_{act}$ became more alkaline. The authors conclude that concentration of 25 mg/m$^3$ acetic acid fumes is a threshold value from the standpoint of acid-base equilibrium in the blood.

Table: Changes in parameters of acid base balance and blood gases

P1116(24/89)* Sosnovskiy AV.
***Combined effects of elevated concentrations of carbon dioxide and environmental temperature on the thermal status of humans in airtight environments.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 89-90; 1989.
[6 references; 2 in English]

Operational Medicine, Thermal Status
Humans
Habitability and Environment Effects, Airtight Environment, Hypercapnic Atmosphere, Elevated Temperature

Abstract: This work involved a physiological/hygienic evaluation of human thermal status during habitation of an airtight space with elevated atmospheric $CO_2$, temperature, and humidity. Subjects were two groups of five healthy males spending 5 days in an airtight space 50 $m^3$ in size. Microclimate parameters were: temperature — 26-28° C; relative humidity — 70-85%; barometric pressure — 740 - 770 mm Hg; $CO_2$ — 3 -3.5%; $O_2$ — 20-21%; with the remainder nitrogen. Parameters measured included: oral temperature, skin temperature at six points (from which weighted average was computed); mean body temperature; heart rate; and respiration rate. Rectal temperature, computed from oral temperature, was used as an estimate of core temperature. Student's t was used to test data for significance.

Under the experimental conditions, skin temperature in the distal portion of the body rose significantly, while that of the back, chest and thigh did not. Rectal temperature decreased by 0.5°, while mean skin temperature increased by 0.7°, causing mean body temperature to remain constant. Decrease in rectal temperature in spite of increases in environmental temperature is attributed to increased $CO_2$ levels. The author cites the following conclusion: 1) observed increase in skin temperature is the result of the effects of all experimental conditions studied; 2) hypercapnic vasodilation of the skin facilitates increased heat emission by the subjects; 3) the increased $CO_2$ concentration decreases the core temperature of humans under conditions of increased temperature and humidity.

Table: Parameters characterizing the thermal status of experimental subjects

**PAPERS:**

P1127(24/89) Myasnikov VI, Ryzhov BN.
***Work and rest schedule and efficiency of operator performance.***
In: Функциональные Состояния и Эффективность Деятельности Человека-Оператора в Режиме Непрерывной Деятельности=Funktsional'nyye Sostoysniya i Effektivnost; Deyael'nosti Cheloveka-Operatora v Rezhime Nepreryvnoy Deyatel'nosti [***Functional State and Efficiency of Human Operator Performance on Uninterrupted Work Schedules].*** Moscow: Institute of Psychology, USSR Academy of Sciences, 1987.
92-110.

Human Performance, Biological Rhythms, Operator Performance, Efficiency; Psychology, Stress
Humans, Males and Females
Work-Rest Schedules, Shifted, Sleep Deprivation

Abstract: The objective of this study was to determine the efficiency of task performance of operators exposed to simulation of altered work schedules such as might occur on space flights. Methods for overall analysis of operator performance were used in two studies differing in type of schedule manipulation. In the first, subjects performed on a 72-hour uninterrupted work schedule (sleep deprivation). Participants were two males aged 33 and 53, and one female aged 39. Operator task involved control of a moving object with 6 degrees of freedom. The subjects were preadapted to conditions inside a pressurized environment with a closed life support system. The 72-hour period of wakefulness began at 7:00 and ended at the same hour 3 days later. During the period, each operator worked on five different training and control tasks, each of which lasted for 20 minutes. Performance level was evaluated on the basis of cumulative assessment of the discrepancy between actual and required object position along each coordinate with respect to the standardized maximum acceptable discrepancy. Psychophysical cost of performance was evaluated using the methodology of integral assessment of stress (G) based on data from heart and respiration rates. Additional data were provided by the results of spectral analysis of EEG. An efficiency parameter was derived by combining performance and stress parameters.

The second study investigated the time course of efficiency of operator performance under conditions of repeated shifts in schedule. Three subjects were used, all males aged 35-54. The study lasted for 30 days. Every 8 days the work schedule shifted by 4 hours, with the first schedule involving start of work at 5:00, the second at 1:00, etc. Measurements were made on the fourth day of each cycle. Operator task involved one-parameter compensatory tracking of a moving object. Task performance occurred in a pressurized environment, but it is unclear whether subjects remained in this environment throughout the 30-day period. Difficulty of tracking task varied. Performance parameters were based on assessment of magnitude of discrepancy in object position. Aside from the physiological parameters measured in the first experiment, galvanic skin response and electromyograms were recorded for the left hand (not involved in task performance).

In the first study, no individual differences were manifest during the first 24 hours of work and performance level was high, no different than baseline. In the EEG records, theta rhythms predominated. Before the work shift started on the second day, all subjects showed signs of fatigue, in which there was considerable individual variance. On the second day performance remained rather high, but there was a general tendency for its pscyhophysiological cost to increase, lowering efficiency score. The most characteristic phenomenon occurring on the third day was a tendency for the parameters of relative stress (difference between stress during performance and during rest) to decrease and even for performance stress to be lower than rest

stress, suggesting inappropriate reactivity. One of the three subjects (the female) maintained a high performance level even on day 3, but her general physiological state during this time was unsatisfactory; she showed signs of extreme fatigue although she did not acknowledge them. Individual differences are attributed to motivational differences as well as gender. On day 3, estimated efficiency decreased by 20% relative to day 1.

Shifting schedules by 4 hours every 8 days had a significant effect on operator efficiency. After each of the first two shifts (starting at 5:00 and then 1:00) performance level decreased (compared to the previous shift) and cost increased, leading to decreases in efficiency. Worst parameter values were recorded between 1:00 and 4:00. Performance level began to improve after the third and fourth shifts. Stress increased after the first and second shifts and then decreased, even dropping below baseline in two subjects after the last shift. During the baseline study and the first shift of schedule, increased tempo of work led to proportionate increases in stress. During the second shift the strength of this association abated, and during the third and fourth there appeared to be a tendency for this reaction to extinguish.

The authors conclude that a phase shift in active wakefulness to the early morning gave rise to biorhythm disadaptation, leading to a sharp decrease in performance efficiency due both to performance decrement and increase in the psychophysiological cost of performance. This was most severe during the second shift, which required subjects to work at night. Beginning after the third shift, efficiency was restored, although objective and subjective evidence indicates that this is an unstable and contradictory process. During this period subjects reported the highest levels of sleep disturbance, apathy, and lack of interest in work, accompanied by decrease in stress level. Work after the fourth shift (starting at 17:00) was better from the standpoint of biological rhythms and this was reflected in recovery of performance and efficiency. However, the inappropriate psychophysiological response to changes in work tempo and the sub-baseline level of working stress testify to the accumulation of fatigue.

The authors conclude that 48 hours of sleep deprivation do not seriously depress operator performance, due to increases in expenditure of effort (cost). Prolonging sleep deprivation to 72 hours leads to a sharp (25%) decrease in efficiency, and inappropriate levels of working stress and/or symptoms of extreme fatigue. Four-hour shifts in work schedules (so that the new schedule starts earlier) decrease (by 20-25%) efficiency of operator performance, especially when work is scheduled for the night hours. Continued forward shifts in schedule (so that work starts in the daylight hours again) lead to relative stabilization of performance and stress parameters, but also to signs of asthenization, such as sleep disturbance and inappropriate psychophysiological response. These data are intended for use in developing work-rest schedules for spacecraft crews who cannot maintain a normal schedule.

Figure 1: Changes over time in parameters of level and efficiency of operator performance during a period of 72 hours of sleep deprivation

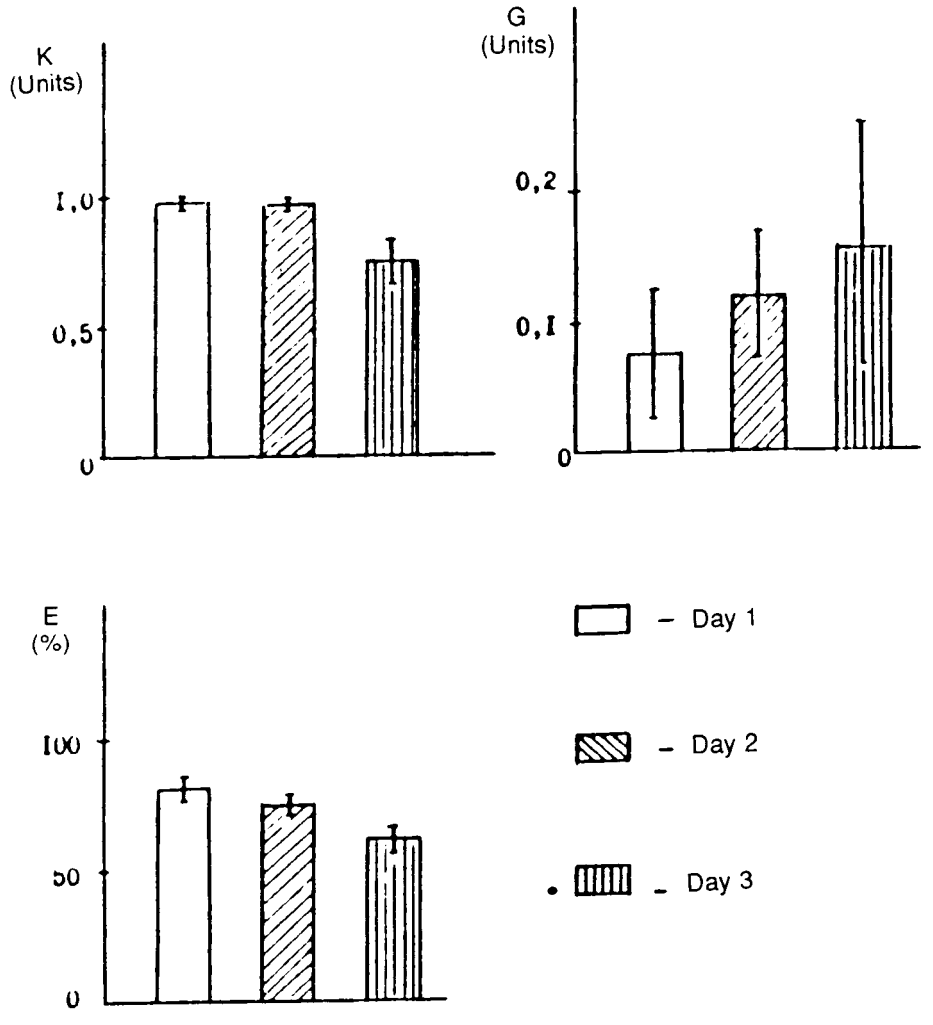


Figure 2: Changes over time in mean group values for parameters of performance level (L), stress (G), and efficiency (E) during performance of operator tasks during a 3-day period of sleep deprivation

Figure 3: Changes over time in increases in level of psychophysiological effort (Δ G) relative to level at rest for 3 days of the experiment during performance of multiparameter compensatory tracking

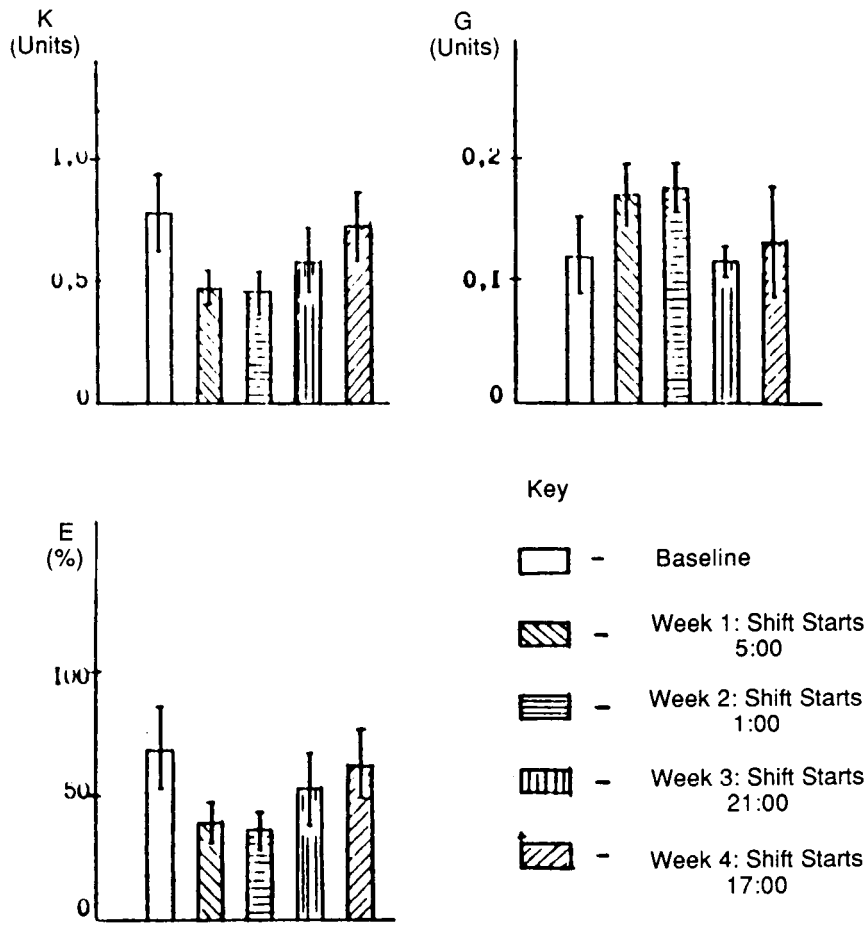


Figure 4: Changes over time in mean group values of parameters of level (L), stress (G), and efficiency (E) during performance of compensatory tracking under conditions of shifts in work schedule

Figure 5: Psychological stress as a function of information presentation rate in operator 3 during weeks 1 and 4 of work

## IMMUNOLOGY

**PAPERS:**

P1123(24/89) Konstantinova IV.
***Manned space flights and the immune system. Long-term flights.***
In: Konstantinova IV.
Sistema Immuniteta v Ekstremal'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммунитета в Екстремальных Условиях Космическая Иммунология ***[The Immune System Under Extreme Conditions: Space Immunology]*** No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology].
Moscow: Nauka; 1988.
Pages 73-104

Immunology. Cellular and Humoral, Allergy
Humans, Cosmonauts
Space Flight, Long-Term, Salyut-4, -6, -7

Abstract: This chapter covers the immunological investigations performed on Soviet manned space flights between 1973 and 1986. At the beginning of training of the first Salyut-4 crew, crewmembers' immune systems were studied using the PHA-blast transformation method and autoradiographic evaluation of two parameters: T-cell reactivity (based on incorporation of $^{3}$H-uridine during early stages of cell culturing with mitogens) and the proliferative potential of T-lymphocytes (based on incorporation of $^{3}$H-thymidine after 48 hours of cell cultivation with PHA). Sensitization of lymphocytes to a number of allergens was also investigated. The humoral system of immunity was assessed by determining the concentration of B-lymphocytes using the immunofluorescent method and by measuring levels of immunoglobulins in serum.

The set of immunological methods used to study Salyut-6 crews included PHA-reactiivity, immunoglobulin and allergen tests, spontaneous E-rosette formation (RF), measurement of active E-rosette-forming cells (E-RFC) and cells forming rosettes in response to sheep antibody comples (EAC-RFC), and also measurement of concentration of B-lymphocytes using the immunofluorescent method. Two autoimmune tests were administered: measurement of titer of antibodies to uncoiled DNA and IgM-autoantibodies against human gamma-globulin, and the latex test for the Rheumatoid Factor. Additional allergy tests observed sensitivity to chemical allergens. Instead of measuring MIF (Macrophage Inhibitory Factor), the studies measured inhibition of leukocyte migration (LIF). For the last two flights of Salyut-6 (1979-1981) the set of methods used to test immune status was expanded through the addition of three tests: assessment of T-helper activity; nonspecific ConA-induced suppressor activity of T-lymphocytes; and cytotoxic functions of natural killer cells. In some cosmonauts, capacity of peripheral lymphocytes to synthesize interferon was studied. A portion of mononuclear cells was incubated *in vitro* for 48 hours in the presence of inactivated Newcastle Disease Virus, an interferon inducer.

The four Salyut-7 flights occurred in 1982-1985. Additional immunological tests performed on their crews included induction of *in vitro* synthesis of interleukin-2 and interferon $\alpha$ and $\gamma$ by lymphocytes. Interferon-$\alpha$ was induced using Newcastle's Disease Virus and interferon-$\gamma$ by concanavalin A (ConA). Activity of natural killers was additionally evaluated through the method of killer-target interaction in a thin layer of agar. Natural killer phenotypes OKT4+ and OKT8+ were also measured.

The most interesting data regarding PHA-reactivity were obtained from considering rates of RNA synthesis in 24-hour cultures containing PHA. This value is very stable in healthy men aged 20-45. The value was depressed in 20 of 25 cosmonauts completing flights of a month or more, dropping from a preflight mean of 19.5 to 10.6 on day 1 after reentry. The parameter

was within normal limits on days 7-9 postflight, and was equal to preflight on day +24-30. The amount of the drop varied. For flights shorter than 120 days, there was no association between flight duration and extent to which this parameter changed. For flights longer than 120 days but below 8 months, all cosmonauts but one showed decreased values on the PHA test, and in five cases the decreases were quite large. For the two longest flights, decreases were more moderate. It is possible that these data show the beginning of adaptation. This, combined with the relatively rapid normalization of this parameter postflight, indicated that the processes causing the phenomenon are reversible.

When DNA synthesis rates were studied on the basis of incorporation of $^{3}$H-thymidine, the parameter was found to be depressed on day 1 postflight in 7 of 9 subjects.

Spontaneous rosette formation (an indicator of the concentration of T-lymphocytes) was studied on the day of reentry in four cosmonauts, and was depressed in all of them. On day 1 postflight this parameter was below baseline in 7 out of 15 cosmonauts, but recovered rapidly. Concentration of T-lymphocytes as identified through the method of "active" E-rosette formation did not decrease, but actually underwent a short-lived increase in 2 of 10 subjects. Concentration of lymphocytes with receptors to a Fc-fragment of immunoglobulin was studied in all Salyut-6 cosmonauts and was found to remain within normal limits.

Thus, the most common effect of long-term flights on cellular immunity is decreased PHA-induced blast-transformation. In some cosmonauts this occurred even though level of T-lymphocytes remained high, suggesting depression of T-cell functioning. This decrease may be associated with depressed functioning of nonspecific T-helpers, with a depression of interleukin-2 production, and also with disrupted suppressor activity of T-lymphocytes found in some or all of these cosmonauts.

Suppressor activity of T-lymphocytes induced by concanavalin A, as manifested by inhibition of PHA-blast transformation of intact lymphocytes (measured autoradiographically), is very stable in healthy subjects. In six of the cosmonauts studied, this parameter was virtually unchanged, while in three others there was an increase in nonspecific suppression and in four there was a decrease [Note: numbers do not add up; in a previous section the numbers are 4, 4, and 4]. The authors postulate that differences in response may be due to specific characteristics of specific flights. No association was found between direction or magnitude of effects and flight duration.

Functional activity of T-helper lymphocytes was studied through the use of a xenogenic graft vs. host reaction. Eight (possibly out of 10) cosmonauts displayed decreases in this index of proliferation.

Activity of natural killers was studied in 15 cosmonauts on flights varying in duration from 65 to 237 days. On day 1 postflight, the index of cytotoxicity was depressed in all 15. Preflight this index averaged 40.6 and on day 1 postflight the average was 11.7; average value on day 7 was 15.1, but the parameter ultimately normalized. In some subjects the index was at a minimum on the first day and gradually normalized; in others, the index continued to decrease during the first week postflight.

Two cosmonauts were studied for activity of natural killers at the level of formation of conjugates of effector cell/target cell, using the method of cytotoxic reaction in agar. The percentage of pairs decreased from 11 to 2 for one and from 26 to 4 for the other on day 1 postflight and remained low on day 7.

Production of interleukin-2 and interferon-$\alpha$ and $\gamma$ were studied postflight in five cosmonauts, in space for 60, 125 and 168 days. All subjects showed a decrease in interleukin-2 production. Interferon formation also decreased.

Total concentration of B-cells identified by the presence of immunoglobulin receptors on their surface decreased on day 1 postflight in two of the four cosmonauts studied. This parameter eventually normalized. Measurement of B-cells by the method of EAC-rosette formation revealed decreases below the norm in 2 of 12 cosmonauts studied. No effects were found in the number of lymphocytes with Fc-fragment receptors.

Few changes were noted postflight in immunoglobulins in blood. The most common effect was a short-term, reversible increase in levels of IgA and/or IgG. Immunoglobulins were studied during space flight, once on day 13 and once on day 53 of the flight of crew 5 on Salyut-6. In the cosmonauts studied on day 13, IgA was elevated to different degrees. IgM was unchanged at this time. On day 52, IgA was within normal bounds in both subjects, but in both IgM had doubled. During the 211-day flight, immunoglobulins were analyzed on days 44, 98, and 198. IgM was elevated in both cosmonauts on day 198, while IgA was within normal limits at all points. Measurements were also made on days 104 and 223 of the 237-day flight. IgM was elevated in one subject on day 104.

The majority of responses to autoimmune tests were negative pre- as well as postflight. One subject who showed presence of Rheumatoid Factor in his blood preflight had even higher levels on day 8 of recovery.

Studies of responses to allergens revealed signs of sensitization in 4/8 cosmonauts (two participated in long-term flights twice). Four developed new responses (two to streptococci and one to formaldehyde) and two showed activation of earlier sensitization to bacterial allergens. One after his first flight on Salyut-6 showed no change, but after a second, longer flight (140 days) displayed increased hypersensitivity to streptococci and staphylococci.

Another study demonstrated sensitization to formaldehyde in three subjects. Formaldehyde alone induced a responses after the 175-day flight. On the 185-day flight there was also a response to epichlorohydrine. No other allergens present in inhabited airtight spaces evoked positive response. The authors conclude that these results suggest that allergic responses increase with flight duration.

Table 2: Functional activity of natural killers and activity of natural killers at the level of formation of conjugates of effector- and target cells in cosmonauts after space flight varying in duration on Salyut-7

| Flight duration | Cosmonaut | Preflight (L-30) | | | | Postflight day 1 | | | | Postflight day 7 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | IC | KE/KT | CCPr | NK | IC | KE/KT | CCPr | NK | IC | KE/KT | CCPr | NK |
| 65 | 1 | 38.8 | 18.0 | 17.2 | 3.1 | - - | - - | - - | - - | 5.2 | 6.0 | 24.9 | 1.2. |
| | 2 | 95.6 | 26.0 | 21.9 | 5.7 | - - | - - | - - | - - | 0 | 12.0 | 48.2 | 4.4 |
| 120 | 1 | 14.4 | - - | - - | - - | 0 | - - | - - | - - | 8.0 | - - | - - | - - |
| 125 | 2 | 46.3 | 24.0 | 35.0 | 8.4 | 0 | 4.0 | 75.0 | 3.0 | 29.9 | 8.0 | 27.0 | 2.2 |
| | 3 | 54.3 | 11.0 | 50.9 | 5.6 | 0 | 2.0 | 72.0 | 1.4 | 34.5 | 6.0 | 22.5 | 1.3 |
| 168 | 1 | 10.4 | - - | - - | - - | - - | - - | - - | - - | 6.4 | 11.0 | 55.3 | 5.0 |
| Statistical Parameters | n | 6 | 4 | 4 | 4 | | 2 | 2 | | 6 | 5 | 5 | 5 |
| | M | 43.3 | 19.75 | 31.25 | 5.7 | | 73.5 | 2.2 | | 14.0 | 6.6 | 35.58 | 2.88 |
| | σ | 30.99 | 6.75 | 15.11 | 2.16 | | 2.12 | 1.13 | | 14.42 | 2.79 | 15.06 | 1.73 |

IC- Index of cytotoxicity; KE/KT - killer-effector/killer-target, % pairs; CCPr - cytotoxic cells in pairs, %; NK - Natural killer cells, %

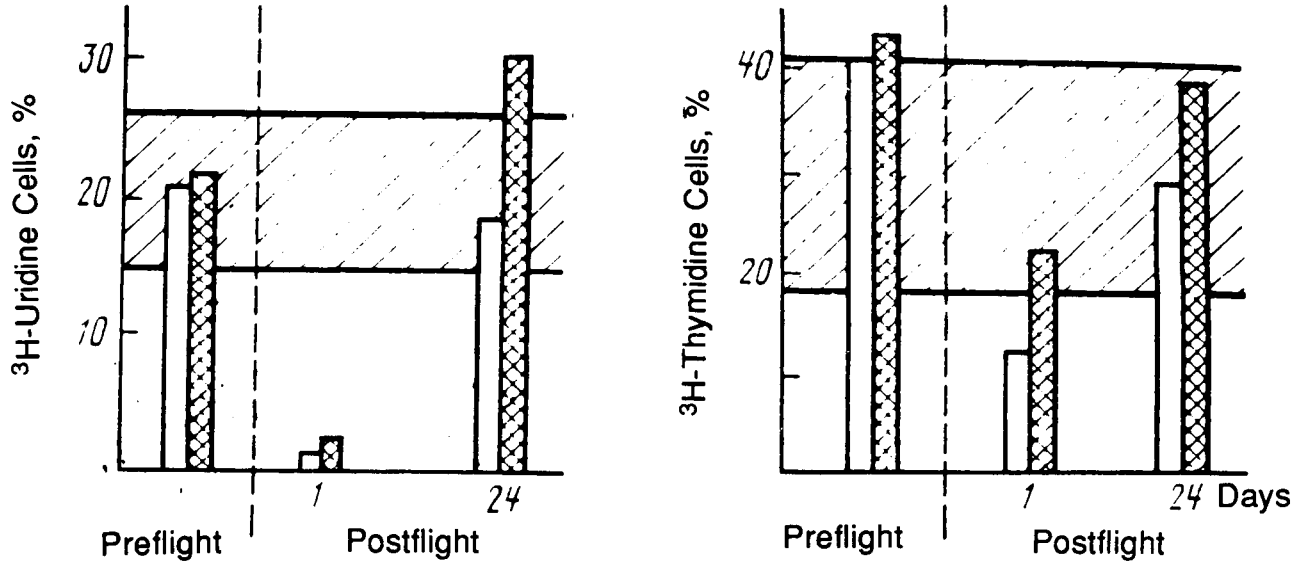


Figure 6: PHA-reactivity of lymphocytes of two cosmonauts before and after an orbital flight lasting 140 days.

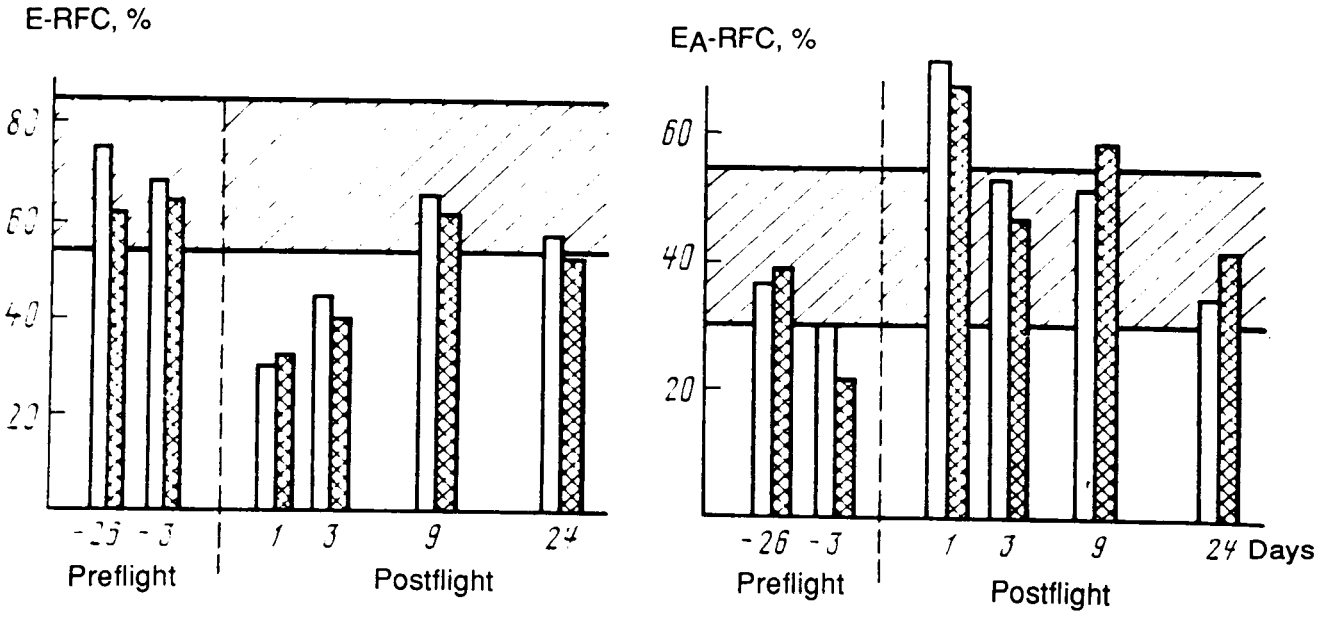


Figure 7: Concentration of E-RFC and "active" E-RFC in two cosmonauts before and after a space flight lasting 140 days

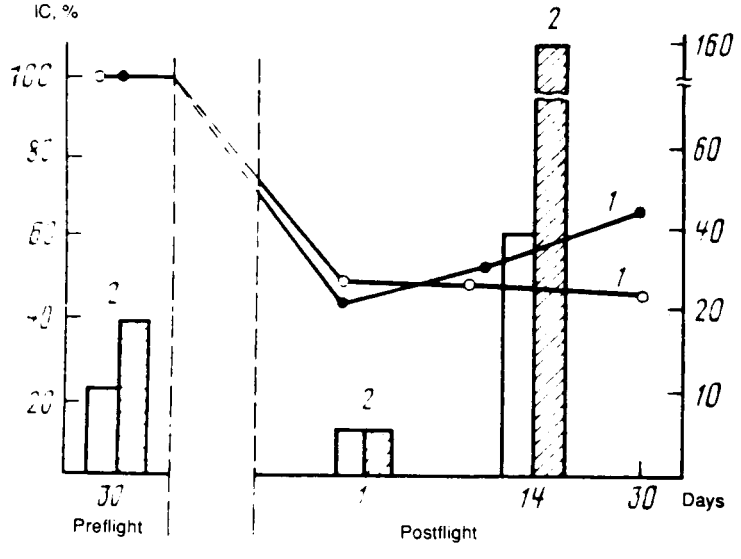


Figure 8: Activity of natural killers (index of cytotoxicity, %) and interferon producing capacity of lymphocytes in two cosmonauts before and after a 75-day space flight
1- cytotoxicity index of natural killer cells; 2 - level of interferon

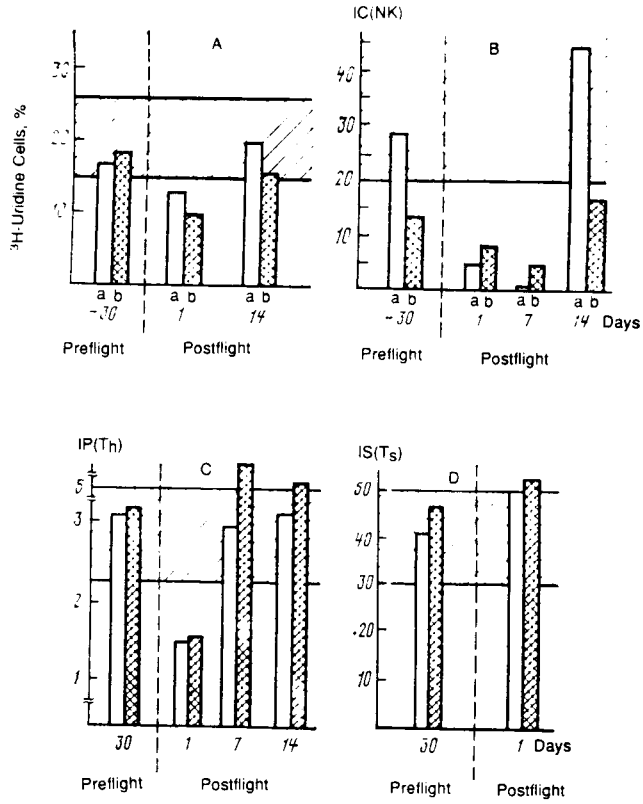


Figure 9: Immune parameters in two cosmonauts before and after a flight lasting 211 days a- PHA-reactivity of lymphocytes. b - index of cytotoxicity of natural killers, c - activity of T-helper lymphocytes (index of proliferation in a xenogenic transplant vs. host reaction), d- activity of ConA-induced suppressors (suppression index, %)

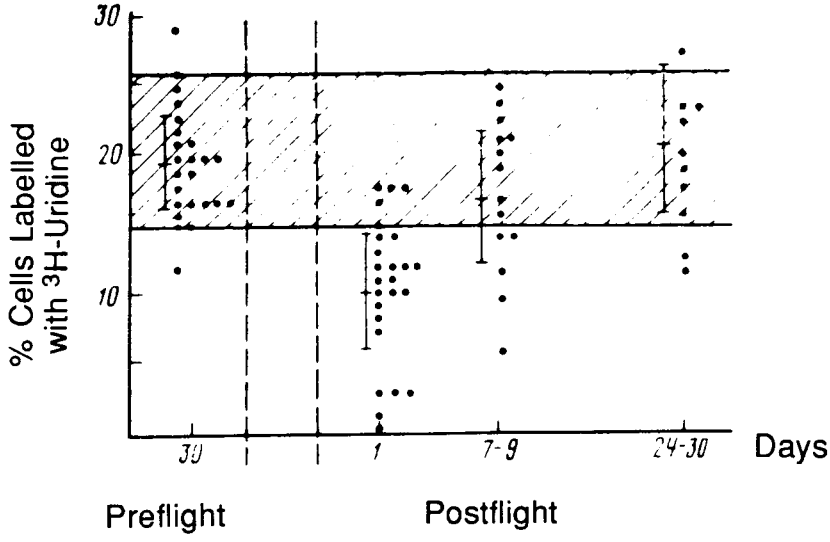


Figure 10: PHA-reactivity after long-term space flights on Salyut-6 and -7 lasting 65 to 237 days

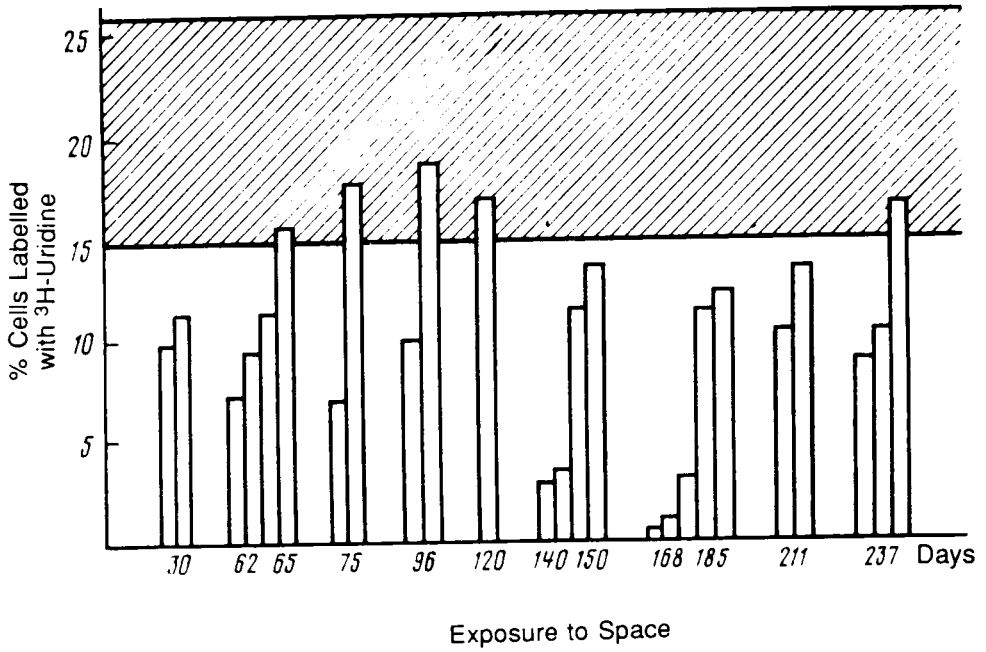


Figure 11: PHA-reactivity of lymphocytes estimated from rate of synthesis of RNA in 24-hour PHA cultures of cells from the blood of cosmonauts exposed to space flight varying in duration. Autoradiographic method.

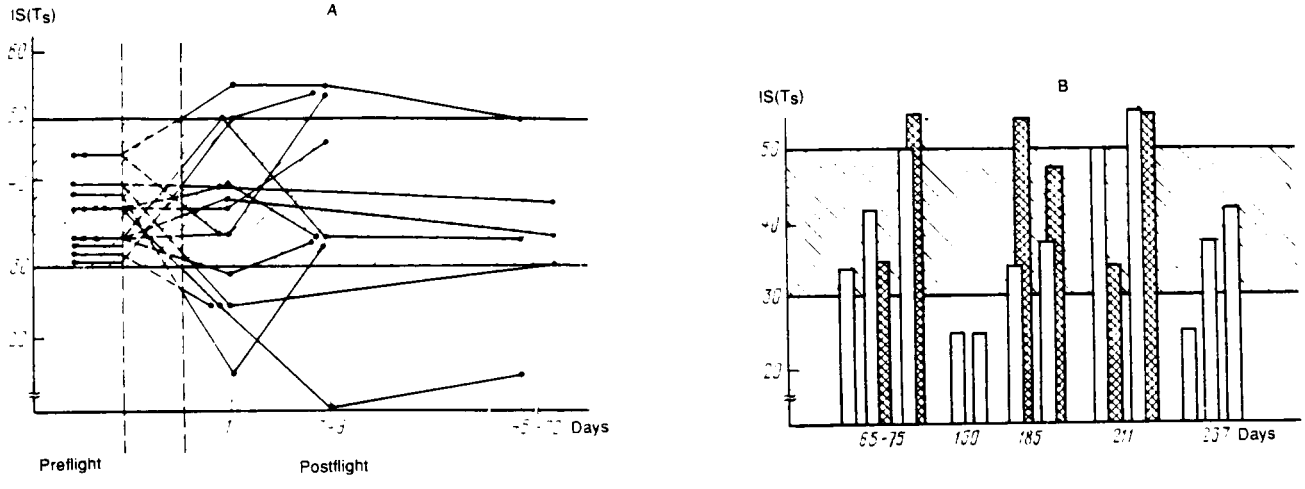


Figure 12: Nonspecific ConA-induced suppression of lymphocyte activity in cosmonauts after long term space flights
A - changes in individual parameters over time; B - value of parameters for different flight duration (white columns - day 1 after reentry; crosshatched columns - day 7)

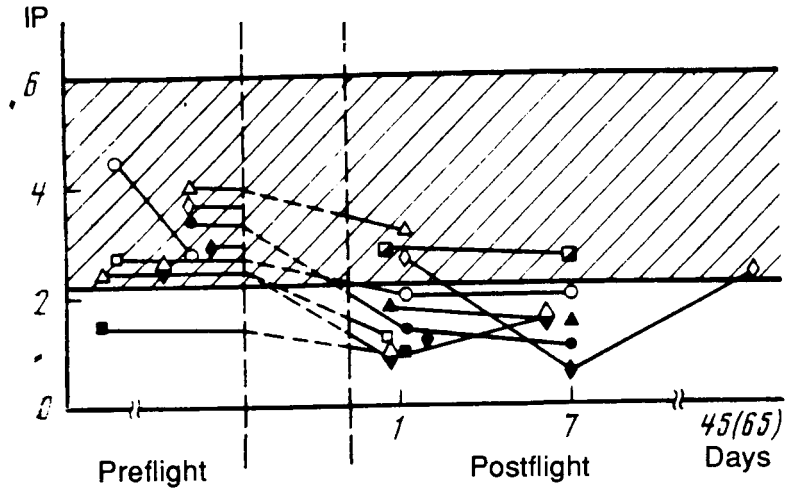


Figure 13: Functional activity of T-helper lymphocytes (index of proliferation with a xenogenic transplant vs host reaction) in cosmonauts after long-term space flights lasting 75 to 237 days.vChanges in individual parameters over time.

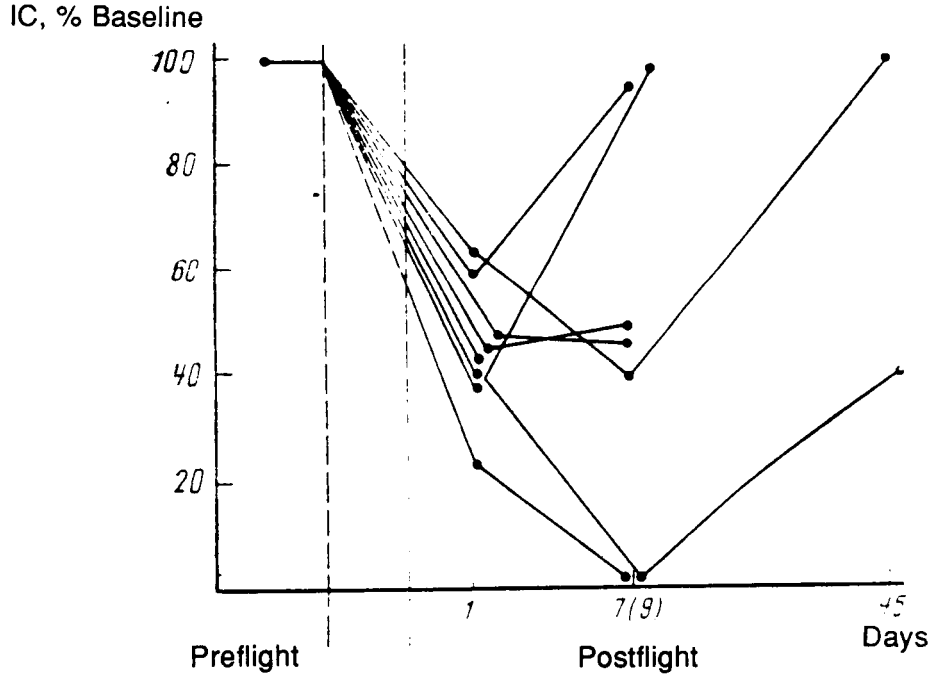


Figure 14: Changes in individual parameters of natural cytotoxicity of natural killers in cosmonauts after long-term space flights lasting from 65 to 237 days

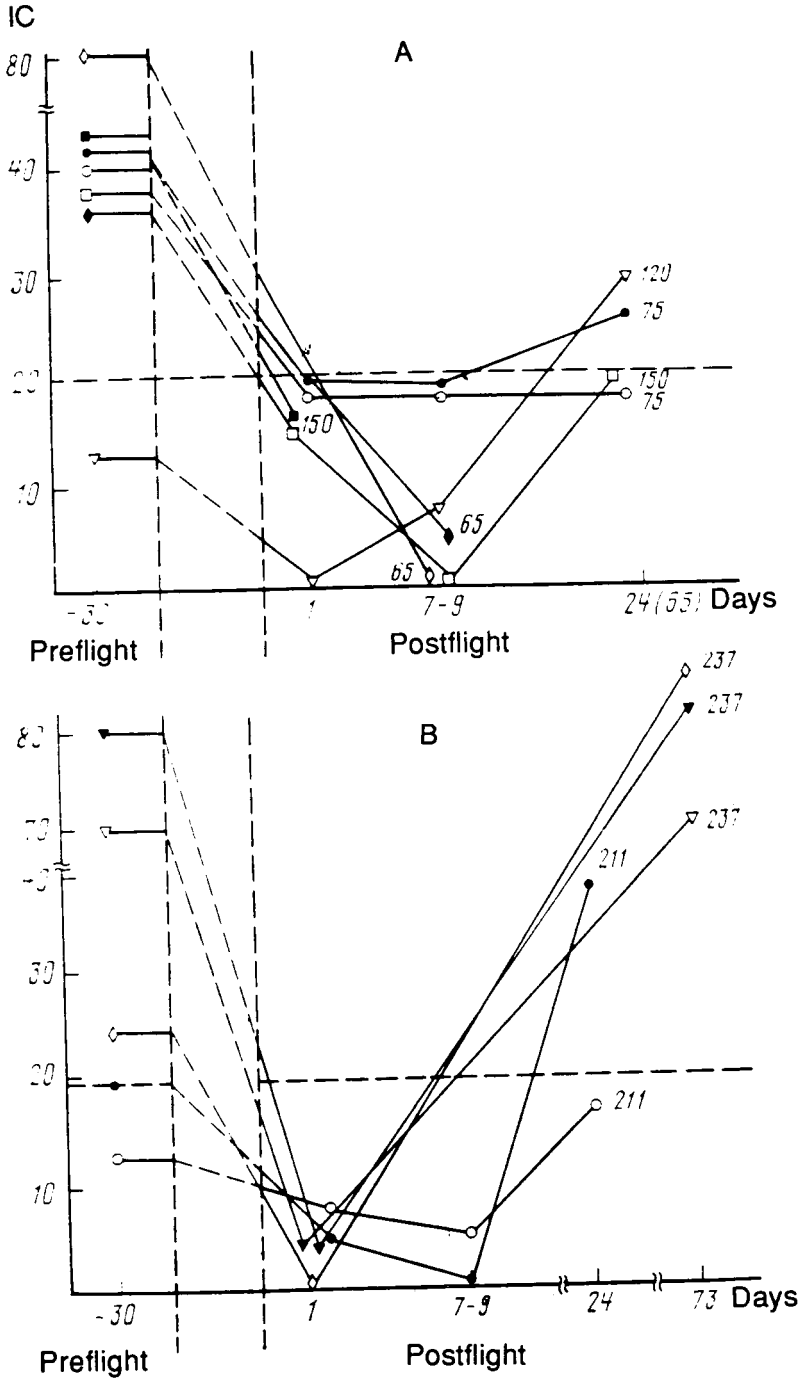


Figure 15: Comparison of decrease in the index of cytotoxicity of natural killers in cosmonauts exposed to space flight for 65-150 days (A) and 211-237 days (B).

Horizontal dotted line represents lower boundary of norm

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***Manned space flights and the immune system. Short-term flights.***
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Moscow: Nauka; 1988.
Pages 104-124

Immunology, Cellular, Humoral, Allergy
Humans, Cosmonauts
Space Flight, Short-Term, Salyut-6, -7, Soyuz

Abstract: The author proposes that the study of human immune reactivity after short-term (7-9 days) flights provides information about the early stages of adaptation to new environmental conditions. To a greater extent than those of long-term flights, results of short-term flights predominantly reflect effects of weightlessness, as opposed to concomitant factors of space flight. Immune responses were studied in 10 visiting crews of Salyut-6-Soyuz and 4 visiting crews of Salyut-7.

PHA-reactivity of T-lymphocytes estimated from rate of RNA synthesis in 24-hour PHA cultures remained within normal limits for 16 of the 18 cosmonauts studied. This parameter was depressed in the early postflight period in two cosmonauts, in one of whom the decrease was not statistically significant. The one cosmonaut in whom this parameter was substantially depressed showed signs of recovery after 1 week.

Proliferative activity of T-lymphocytes was unchanged in 15 of 16 cosmonauts studied. The exception was the cosmonaut who displayed depression in RNA synthesis, although this parameter too showed signs of normalization 1 week postflight. Level of E-RFC was depressed in 9 of 27 cosmonauts studied. However, "active" T-lymphocytes were elevated in 5 of 20. Nonspecific suppressor activity of T-lymphocytes was virtually unchanged in 12 of 13 individuals studied, and elevated in 1. Functional activity of T-helper lymphocytes (amplifiers) was depressed postflight in a significant portion of cosmonauts. The group mean, which 60 days before launch had been 3.6, dropped to 2.3 on the first day after reentry. Individual effects were noted in 10 of 18 cosmonauts.

Natural killer cell activity was studied in 16 cosmonauts after short-term flights. In the majority of cases a high index of cytotoxicity was retained. However, in five there was a short-lasting but reliable decrease on day 1 post flight. Interferon-forming capacity was studied in nine subjects, of whom, as Table 3 shows, six displayed decreased levels of IFN-$\alpha$ on day 1 postflight. In those in whom this effect was studied further, normalization began to occur in the first week. Total concentration of B-lymphocytes did not change in cosmonauts after short-term flights. The proportion of B-lymphocytes with receptors to the third complement component (EAC-RFC) remained normal in most cosmonauts. However, in four this parameter decreased significantly on day 1 postflight. In one subject, the parameter did not normalize until 2 weeks postflight. Concentration of lymphocytes containing a number of other cellular populations, as measured by the presence of receptors to Fc fragment of immunoglobulins. did not change in any subject. Only small changes were noted in immunoglobulins in blood serum in some individuals. Most subjects showed no deviations in responses to autoimmune tests. However, one cosmonaut showed evidence of the rheumatoid factor postflight and two had elevated titers of antibodies to uncoiled DNA. One of the latter complained of feeling ill. None of these effects were present preflight.

Two cosmonauts were studied after participation in a highly stressful 2-day flight, involving, among other factors, lack of sleep. These cosmonauts displayed a drop in PHA-reactivity, along with decreased "active" E-RFC and lymphocytes with complement receptors, increased IgA, and increased IgG (in one of the two). A single cosmonaut responded positively to streptococci allergens, and one to formaldehyde. These responses had not been present preflight.

The author considers the three most important questions about this data to be: 1) What are the features of the set of changes typically occurring when the immune system undergoes acute adaptation to weightlessness? 2) What is the "contribution" of the nonspecific stress component to impairment of immune reactivity after short-term space flights? 3) Are there correlations among the changes identified in various components of the immune system, and what is their clinical significance?

She argues that the best way to answer the first question is to compare results after long- and short-term flights. Most characteristic of the former is drop in PHA reactivity of T-lymphocytes and onset or increase of allergic sensitization to various substances. These changes do not occur after short-term flights. Three other phenomena: decrease of T-cells in blood, decreased T-helper activity and drop in the cytotoxic activity of natural killers are observed after both long- and short-term flights, although they are less severe after the latter. The author concludes that the distinguishing feature of the acute period of adaptation of the immune system to space flight is decreased concentrations of T-lymphocytes in blood without decreased PHA reactivity.

The possibility that effects of short-term space flight on the immune system can be attributed to exposure to the pressurized cabin has been ruled out, since ground-based chamber experiments even with much more adverse environmental parameters do not affect immunoreactivity for short (<9 days) periods of habitation. Experiments inducing emotional stress lead to drops in PHA reactivity, ruling out stress as the decisive factor. Decrease in T-lymphocytes and T-helper activity may possibly result from migration of T-lymphocytes to bone marrow, which occurs in acute or chronic stress situations and their pharmacological simulations (i.e., administration of corticosteroids). Increased numbers of T-lymphocytes in marrow have been observed in rats after short-term flights. However, this hypothesis is by no means proven.

Decreased killer cell activity may relate to reduced synthesis of lymphokines (including interleukin-2) leading to decreased intracellular processes determining level of activity of effector cells. Study of killer cell activity — both recognition of target cell and lysis, performed in a thin agar layer — in a small number of cosmonauts after long-term space flight, yielded the unexpected result that the recognition function was impaired (concentration of lymphocytes in peripheral blood able to recognize targets and form conjugates with them was decreased by a factor of two), while lytic potential was normal. These results are puzzling, since the recognition function is known to be quite resistant and the lytic function rather labile. A hypothesis may be advanced that there is a deficit of mature natural killers entering the blood from bone marrow. These results may be associated with the fact that electron microscopy of conjugates with cell targets in peripheral blood of cosmonauts after short-term flights revealed disruptions of the ultrastructure of the secretory and ultrastructure apparatus of the cells. (See Figures 17-22).

Results from space flights of different durations can be summarized as follows. After a 2-day flight, involving a great deal of stress, but not long enough for habitation conditions to be important, cosmonauts displayed decreased PHA-reactivity of T-lymphocytes and elevated IgA and IgG. However, concentrations of T-cells remained high. After 7-8 day flights, PHA reactivity did not drop, but concentration of T-cells did, and in half the subjects there were significant decreases in activity of natural killers and T-helpers. After longer flights, all six

parameters were affected in the majority of cosmonauts. All aberrations in immune response eventually disappeared postflight.

After short- and long-term space flights the B-cell system was less affected than the T-system. Concentrations of B-cells in peripheral blood and levels of immunoglobulins of various classes were relatively stable. The greatest changes occurred in class A immunoglobulins. The synthesis, secretion, and functioning of IgA are associated with the mucous membranes of the digestive tract and bronchi, with the synthesis of the secretory component, and with the secretion of IgA in bile.

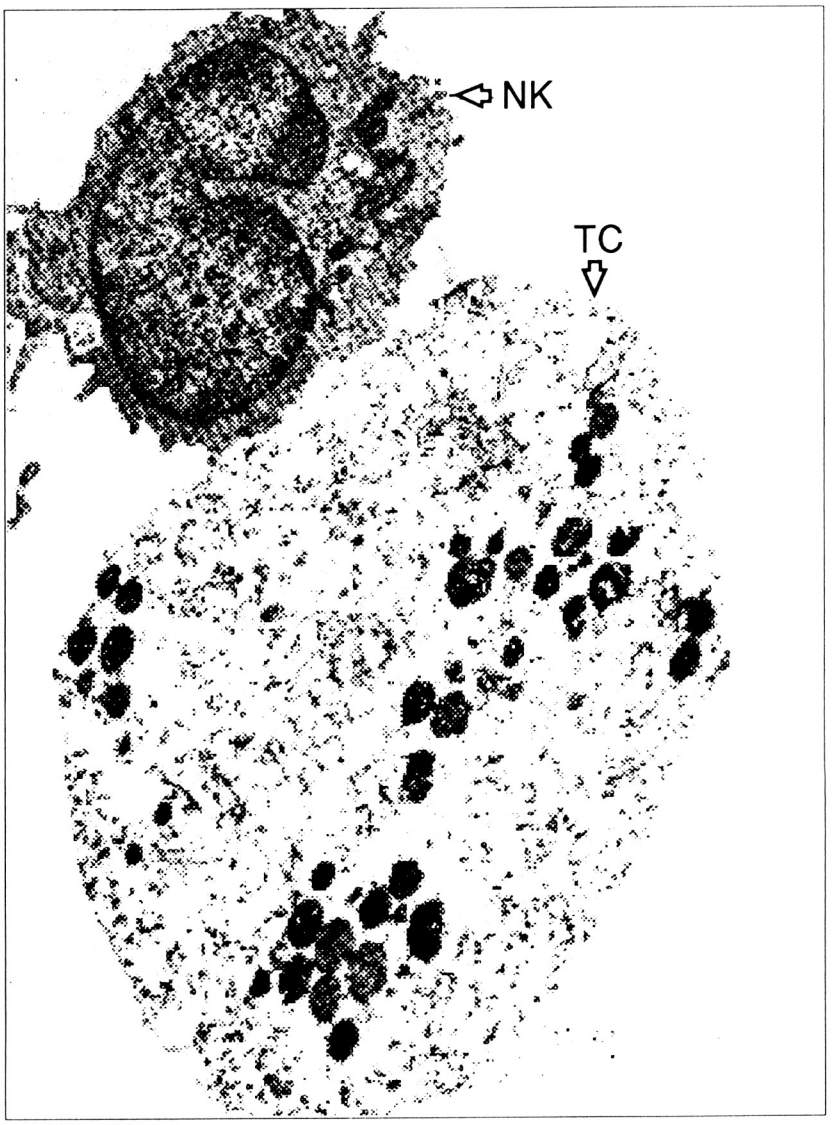


Figure 17: Interaction of a natural killer with a target cell 10 minutes after adsorption

The arrow indicates a portion of the natural killer cytoplasm depicted in Figure 18. NK - natural killer, TC - target cell, X 20,000


Figure 18: Fragment of Figure 17, X 75,000
M - mitochondria, T - tubular structure, GER - granular endoplasmic reticulum

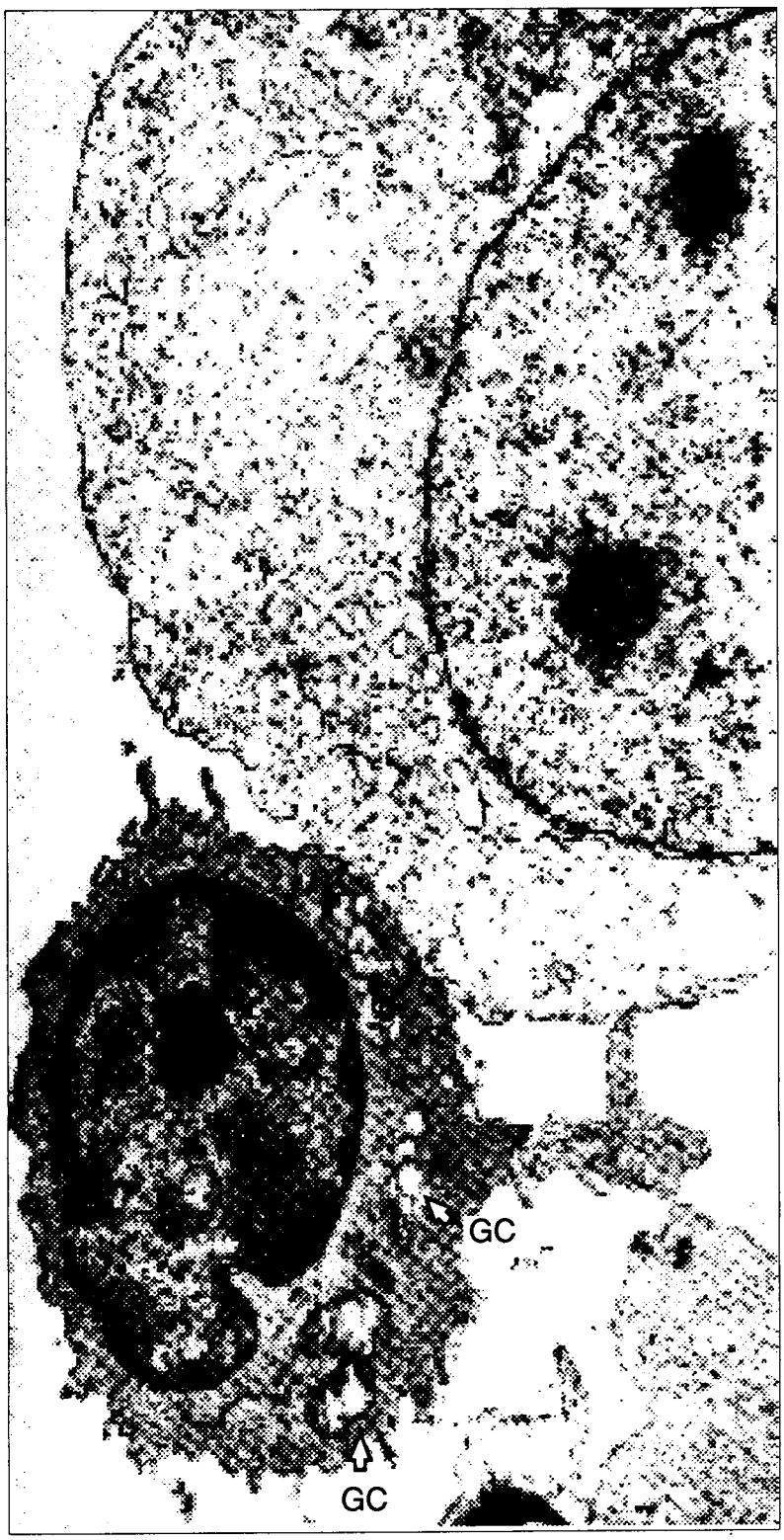


Figure 19: Adsorption of a natural killer on a target cell.
Golgi complex (GC) is localized in the cytoplasm area, far from the contact point of the natural killer and target, X 20,000

Figure 20: Partial activation of secretory apparatus (hypertrophy of the Golgi apparatus in the absence of secretory granules and microtubules), X 75,000

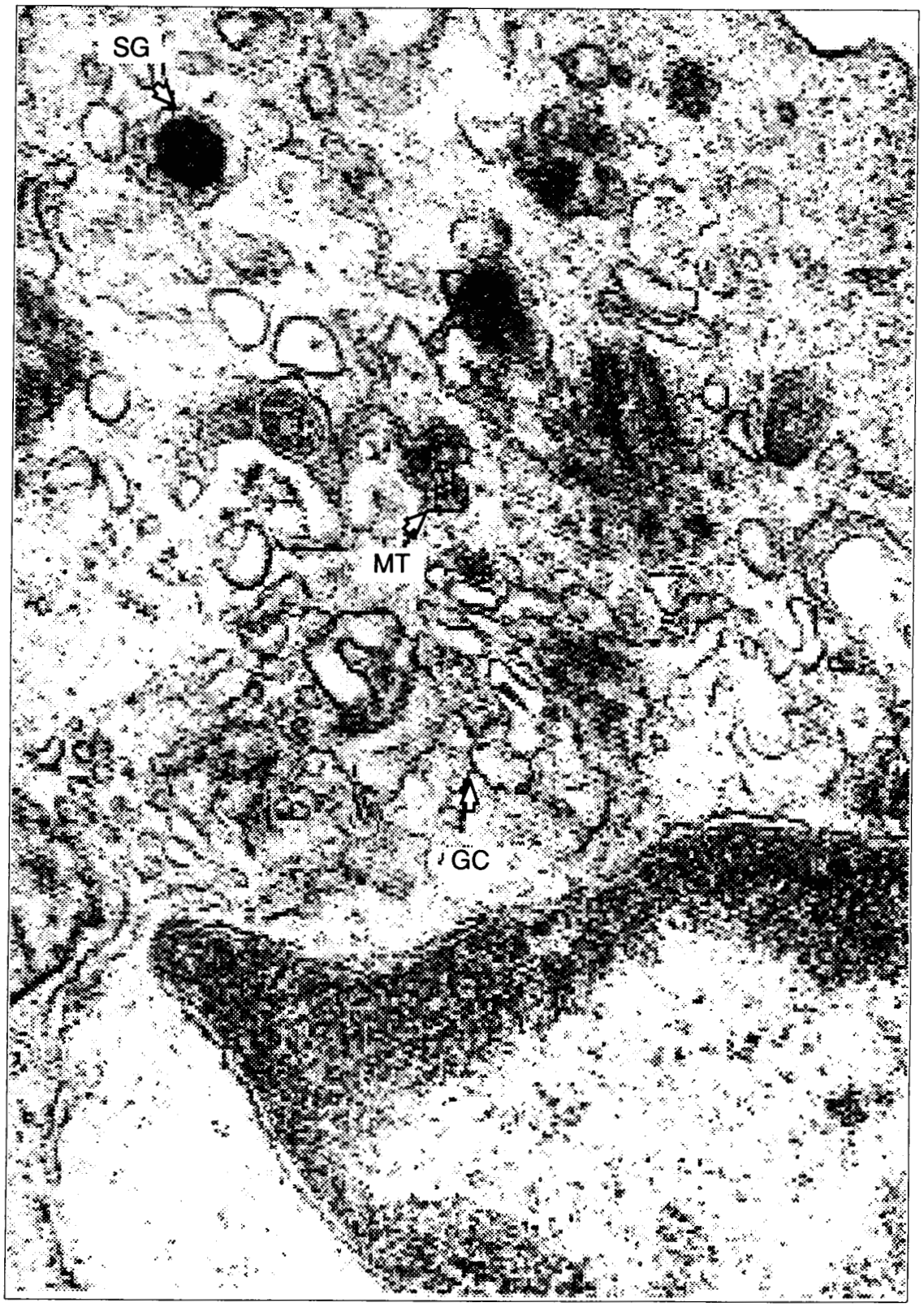


Figure 21: Activation of the secretory apparatus.
GC - Golgi apparatus, SG - secretory granules, MT - microtubule complex

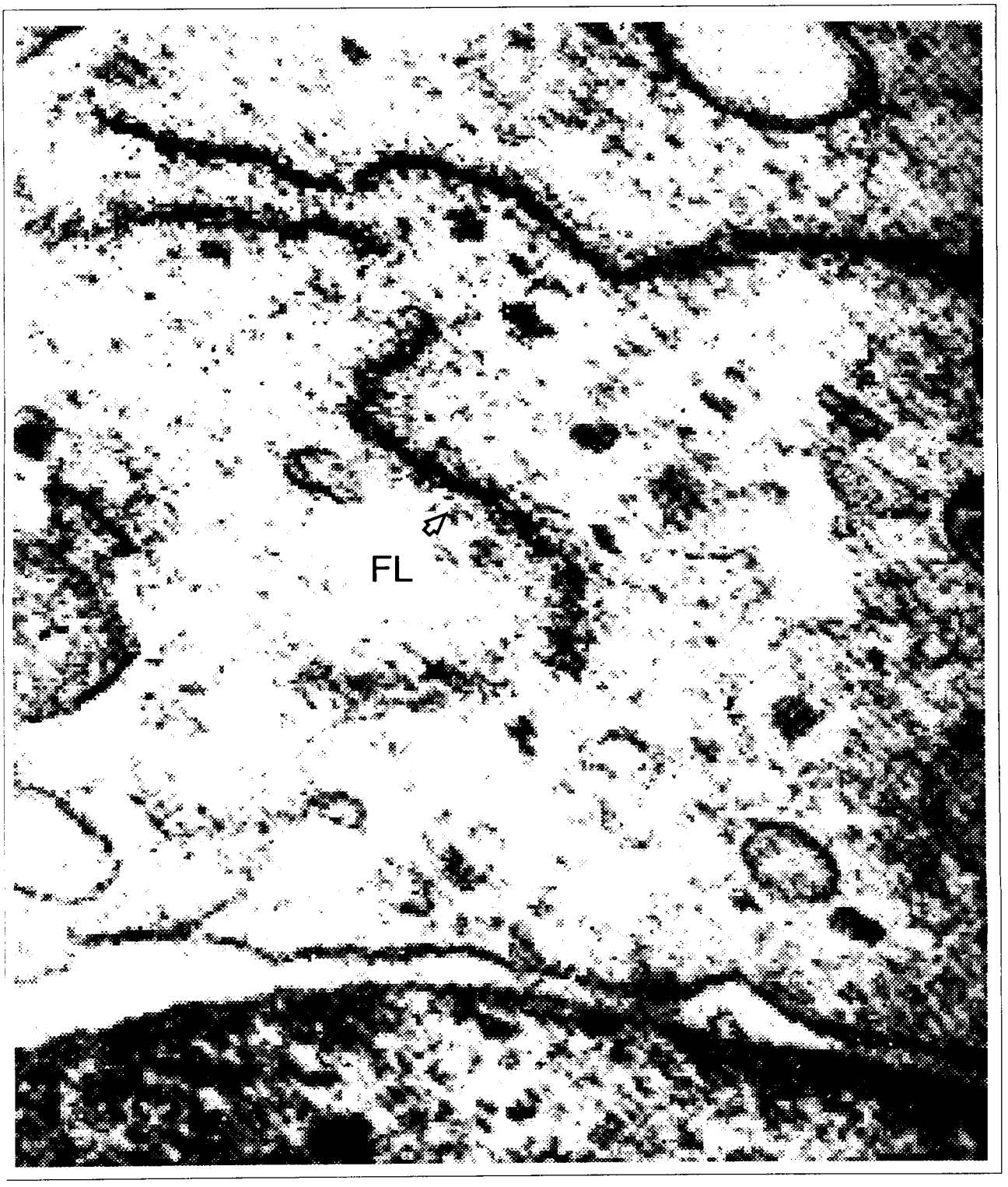


Figure 22: Fragment of Figure 21, X 75,000
Activation of secretory apparatus (does not move to the surface of the natural killer due to the presence of "new" structures): FL - fibrous lamina

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***Space flights of animals on COSMOS biosatellites.***
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Pages 155-174.

Immunology,.Immunity. Cellular, Humoral, Bone Marrow, Lymphatic System, Spleen, Thymus
Rats
Space Flight, COSMOS-605, -782, -936, -1667

Abstract: The majority of rat experiments on COSMOS biosatellites were conducted in modules housing 25 animals individually, with systems for automatic delivery of food and water, ventilation, illumination, waste collection, and monitoring of the condition of the animals on the basis of body temperature and motor activity. After the flights, the animals were in generally satisfactory condition, but showed some signs of sluggishness with decreased general tonus and motor activity. Growth rate of flight animals had slowed compared to that of control rats. Kidney and adrenal weight increased, while that of thymus, spleen, and some muscles decreased. Hematological studies after some flights showed neutrophilia and lymphopenia in the early postflight period. After one flight, leukocytes were depressed, while leukocytosis was noted after others. Some of the immunological experiments performed on COSMOS satellites were conducted jointly with NASA scientists. Aside from the data from cosmonauts described in previous abstracts, early results relevant to the immune status of animals after space flight include the finding that rats flown for 22.5 days on board COSMOS-605 in 1974, showed involutions of the thymus and spleen accompanied by hypoplasia of the red and white splenic pulp.

The joint U.S.-USSR experiment performed on COSMOS-782 focused on the effects of space flight on cellular immunity. Scientists studied the reactions of splenic cells to a specific antigen and nonspecific mitogens. Flight rats (N=16) were injected with 0.2 ml of a formalinized suspension of *Listeria monocytogenes* in a complete Freund adjuvant. Postflight analysis of splenocytes was conducted on the 25th day after immunization. There were three control groups, each containing six rats: the synchronous group was immunized and housed in a satellite mock-up; one vivarium group was immunized and maintained under ordinary laboratory conditions. The second group was not immunized. The animals were sacrificed 9-11 hours postflight (flight duration 19.5 days) and the spleen removed and fixed and transported for laboratory study. Time elapsed between sacrifice and analysis was about 30 hours. The cells were washed and the erythrocytes were removed under conditions of "hypotonic shock." The final dilution of cells was $1X10^6$ live lymphocytes in 1 ml RPMI-1640 medium containing 10% heat-inactivated fresh rat serum. PHA and ConA in two dilutions 1:10 and 1:100 of the initial working solution were used as mitogens. The specific antigen was a suspension of formalinized *Listeria* cells, in a 1:10 and 1:100 dilution in a RPMI-1640 medium. The cytoplasmic *Listeria* antigen was derived from a live growing culture that had been passed through a special device which destroyed the bacteria. The supernatant was separated from the cellular fragments by centrifugation. Protein was measured using Lowry's method. Purified tuberculin was diluted 1:10 and 1:100 in a RPMI-1640 medium. The cells were incubated for 72 hours at 37° in a 5% $CO_2$ atmosphere. During the last 24 hours, 2 μm $^3H$-thymidine was added. After washing, the cells were placed on filters and radioactivity was recorded. The data were expressed in the form of an index of stimulation. This parameter showed that the lymphocytes of flight rats responded well to the nonspecific mitogens and bacterial antigens with which they had been immunized. Variability of response was greater in flight rats than in

the other groups. Rats of the synchronous control showed a depressed response compared to the flight and laboratory control groups. It was concluded that stress had a less pronounced inhibiting effect on immune response in weightlessness than under 1-g. In spite of their unimpaired response, animals of the flight group did display involuted lymphoid organs.

A Soviet experiment on COSMOS-782 investigated the activation capacity of B-cells in response to a polyclonal mitogen (lipopolysaccharide *E. coli*). Reactivity of B-cells is an integral parameter indicative of the state of metabolism of individual B-lymphocytes, as well as of reactivity of the totality of B-lymphocyte clones. Hours after COSMOS-782 landed, flight rats exposed to space for 19 days were sacrificed. In a process taking approximately 36 hours, the spleens were removed, placed in a sterile solution, and, in the case of the flight group, transported to Moscow. Reactivity of splenic lymphocytes was studied in a total of 22 rats. A suspension of splenic cells was prepared on a RPMI-1640 medium containing glutamine, antibiotics and 10% fetal calf serum. The cells of each rat's spleen were cultivated with and without mitogen in a total of six cultures. Cell viability after preparation of the suspension and after completion of the experiment was measured using an eosin test. *E. coli* lipopolysaccharides (ECL) were dissolved in a balanced Hank's salt solution. Then the solution of ECL was dialyzed on a phosphate buffer, and brought to the requisite concentration of the culture medium. Twenty-two hours after the culture had been established ($^3$H-thymidine, 2 μCu/ml, specific activity 5 Cu/ml for 4 hours at 37°), no differences were found between the flight and synchronous control groups. At the same time, the radioactivity of cell suspensions from both these groups significantly exceeded vivarium values, suggesting heightened reactivity of B-cells to ECL. The author hypothesizes that the maintenance conditions in the flight and synchronous groups may have stimulated baseline synthesis of DNA in splenic lymphocytes and thus their reactivity to ECL. This may be a nonspecific stress reaction.

After an 18.5-day flight on board COSMOS-936, rats were examined for level of class G immunoglobulins in blood. In addition, the concentration and avidity of specific and nonspecific clones of B-lymphocytes were studied in the spleen. Rates of RNA and DNA synthesis and total populations of lymphoid cells were also measured. There were 5 animals each in the flight and synchronous groups and 5 in an immunized and 16 in a nonimmunized control group. The animals in the first three groups were immunized 8 days before launch through intraperitoneal administration of 0.7 ml 10% suspension of sheep erythrocytes. Flight rats were sacrificed several hours after reentry, and synchronous rats after a comparable interval. The spleens were removed under sterile conditions and weighed. The portion of the spleen designated for immunological research was used to prepare a cellular suspension, which was transported at the temperature of melting ice. The transport period was approximately 27-29 hours. The proportion of viable cells was 58-64% in all groups. Blood was taken from all animals immediately after sacrifice. Serum was frozen after removal of coagulum. Immunoglobulin G was measured in serum by radial diffusion in gel, using rabbit antiserum against rat $IgG_2$-globulin. Analysis of specific and nonspecific lymphocyte clones in rat spleens included measurement of lymphocyte concentration with immunoglobulin IgM-receptors on the cellular surface. The method of rosette formation with TNP-erythrocytes was used. Conjugated TNP-BSA served as inhibitors for the nonspecific clone and antiserum was used against the light chains of rat immunoglobulins for specific clones. The lymphocytes from each rat were studied individually, with inhibitors used to control the specificity of response. Distribution of avidity of clones of TNP-positive B-lymphocytes was analyzed for the four groups of animals. The reaction of rosette formation with TNP-erythrocytes took place in the presence of increasing concentrations of inhibitor. Inhibition curves were constructed. Rate of synthesis of RNA and DNA in the splenic cells of the animals were estimated on the basis of incorporation of $^3$H-uridine and $^3$H-thymidine. Incubation time of the cell suspension with the isotope was 60 minutes at 37°. Results were obtained through autoradiography. The level of $IgG_2$ in the immunized rats of the synchronous and vivarium group, as well as the nonimmunized group,

were virtually the same. In flight animals the level of IgG was significantly lower. No differences were found between flight and control groups in the two groups of B-lymphocyte clones (TNP-positive and sheep erythrocyte-positive). The level of rosette forming cells (E-RFC) was virtually the same in the flight and synchronous control groups, and was higher than that of non-immunized vivarium animals. No differences were found in avidity distribution of TNP-positive clones of B-lymphocytes. Nor were differences found in rates of RNA and DNA synthesis. The author concludes that the most important shift associated with flight found in this experiment is the decrease in IgG, suggesting attenuation of the specific function of mature B-lymphocytes. The absence of decreased biosynthesis of DNA and RNA suggest that flight factors do not have a marked effect on functioning of the protein synthesizing system of lymphocytes, but may selectively affect biosynthesis of immunoglobulins. Increase in TNP-positive B-lymphocytes, since it occurs in the synchronous as well as flight groups, is attributed to something other than weightlessness.

The objective of an experiment performed during the 7-day flight of rats on COSMOS-1667 was to study the effect of space flight on anti-viral resistance. Immunological parameters were studied in seven animals sacrificed on the first day after reentry, seven vivarium and seven synchronous controls. Material for the studies were mononuclear cells from spleen tissue and bone marrow of subjects. The concentration of T- and B-lymphocytes in the spleen and marrow was determined using immunofluorescence with appropriate antiserums. Proliferative activity of lymphocytes was evaluated in a 48-hour culture of cells with 5 μg/ml ConA on the basis of incorporation of $^{3}$H-thymidine in lymphocyte DNA. Cytotoxic function of lymphocytes of natural killers was observed in a test of natural cytotoxicity using as targets cells of the transplanted K-562 line labelled with $^{3}$H-uridine. Capacity of lymphocytes to synthesize IL-2 was measured in a supernatant of 48-hour cultures of splenocytes incubated with ConA on the basis of their capacity to restore the diminishing proliferation of T-lymphocytes. The latter was evaluated radiometrically based on inclusion of $^{3}$H-thymidine.

Concentrations of T- and B- lymphocytes in the spleens of rats (Figure 34) after a 7-day flight were unchanged. In the bone marrow, B-cells were unchanged, but the amount of T-cells in flight rats was twice as high as in vivarium controls and 1.5 that of synchronous controls. T-cells in spleens of flight rats showed a significant depression in reactivity to ConA compared to that of other groups. Although the flight group had more T-cells in their bone marrow, the functional activity of these cells was the same for all groups. Cytotoxic activity was also depressed in flight rats compared to both controls in both the spleen and bone marrow. Capacity of cells to produce interleukin-2 was below that of control groups for flight rats.

These results, decreased reactivity of T-lymphocytes without decreased quantity, are interpreted as indicating a true decrease in functional activity and confirm the decrease in PHA-reactivity of T-cells noted in humans after space flight. Results also suggest a selective migration of T-cells into bone marrow in the flight animals. Such a phenomenon has been observed after simulated stress and injection of corticosteroids. It is not yet possible to say whether this effect should be associated with weightlessness or reentry factors. Decreased cytotoxicity found in flight rats has also been noted after acute stress, and has been confirmed by work on manned flights.

Figure 34

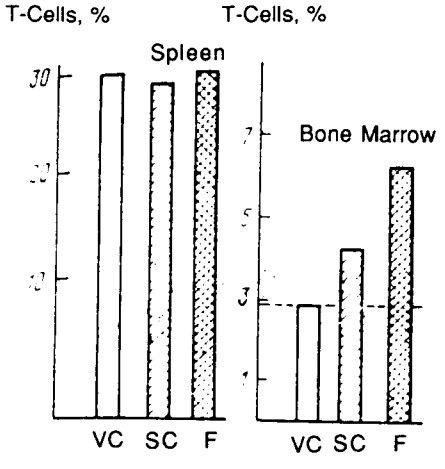



Figure 35

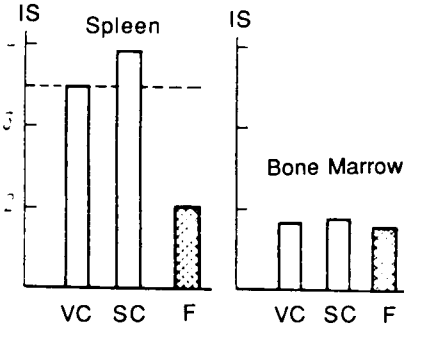



Figure 36

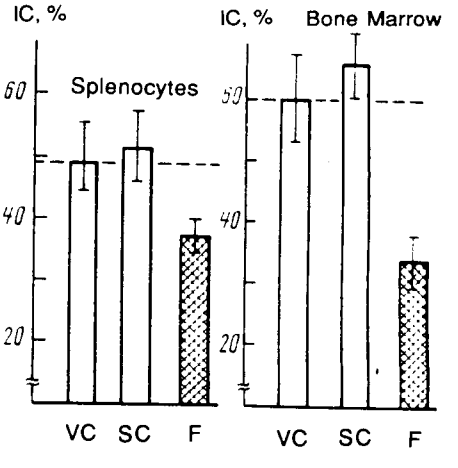



Figure 34: Concentration of T-lymphocytes in the spleen and bone-marrow of rats after flight on biosatellite COSMOS-1667

Here and below: F - flight group; SC - synchronous control: VC - vivarium control

Figure 35: ConA-reactivity of splenocytes and bone marrow cells (index of stimulation) in rats after flight on COSMOS-1667

Figure 36: Cytotoxic activity of natural killers in the spleen and bone marrow in rats after flight on COSMOS-1667

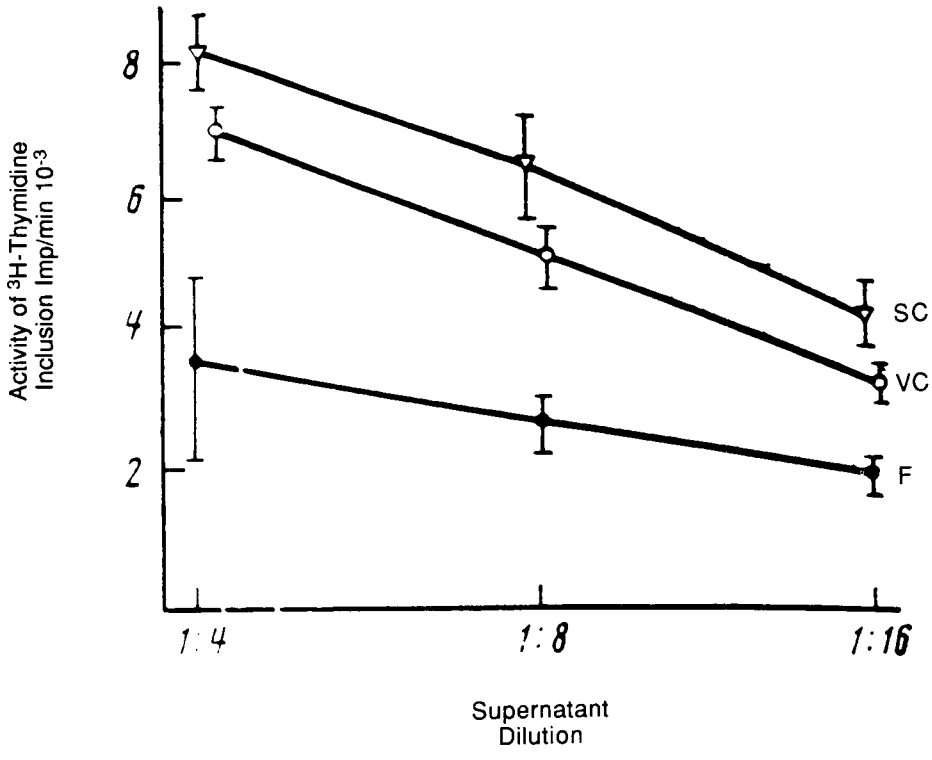



Figure 37: Production of interleukin-2 by cells of the spleens of rats after flight on COSMOS-1667

Table 5: Research on rats exposed to space on COSMOS series biosatellites

| Element | Parameter | Satellite | Scientists |
|---|---|---|---|
| | **Immunological Studies** | | |
| B-lymphocytes | Nonspecific proliferative response B-mitogens of ECI | COSMOS-782 | I.V.Konstantinova, M.T. Martinez, N.N. Sakayan |
| | Level of specific antigens | COSMOS-936 | G.M. Zhuravel', I,V. Spirande, B.B. Fuchs, I.V. Konstantinova |
| | B-lymphocytes with (E-RFC) and without control (TNP-RFC) of receptor nature of recognition | | |
| | Avidity distribution of antigen-specific (E-RFC) and antigen-non-specific (TNP-RFC) B-lymphocytes | COSMOS-936 | B.B. Fuchs, I.V. Spirande, T. Martinez. I.V Konstantinova |
| | Concentration of IgG ($IgG_2$) | COSMOS-936 | V.L. Yurin, N.N. Sakayan. I.V. Konstantinova, B.B Fuchs, N.N. Mukhina, A.D. Mandel, Ye. Beylish |
| T-lymphocytes | Specific proliferative response to Listeria antigen | COSMOS-782 | A.D. Mandel, Ye. Beylish |
| | PHA-reactivity and concentration of T-lymphocytes in spleen and bone marrow | COSMOS-1667 | A.T. Lesnyak N.V. Bozhikov |
| | Induced production of IL-2 | COSMOS-1667 | I.V. Serov |
| Natural killers | Cytotoxic activity of natural killers in the spleen and bone marrow | COSMOS-1667 | M.P. Rykova |
| | **Morphological Studies** | | |
| Thymus, spleen, lymph nodes | Morphological analysis of the organs of the immune system | COSMOS-605 COSMOS-1667 | G.N. Durnova A.S. Kaplanskiy |
| | **Cytochemical Studies** | | |
| Lymphocytes (total pool) | Synthesis of RNA and DNA (autoradiographic analysis) | COSMOS-936 | I.V Konstantinova, N.N. Sakayan |

Table 6: Comparison of morphological changes in lymphoid organs of rats after flight and various ground experiments (from Durnova, 1978)

| Factor | Elapsed time btwn treatment & sacrifice, hrs | Morphological changes in lymphoid tissue |
|---|---|---|
| Weightlessness 18.5-22 days | 4.5 -13 | Acute stress pattern (disintegration of lymphocytes in cortical substance, in lymphoid follicles of the spleen and parafollicular zone of the lymph nodes, neutrophil infiltration of red splenic pulp) |
| Earth - acute stress | Several | Acute stress pattern |
| " " " | 24 and longer | No sign of acute stress |
| Artificial gravity in flight lasting 18.5 days | 4.5-13 | No sign of acute stress |

P1126(24/89) Konstantinova IV.
***Experiments in weightlessness on isolated cells.***
In: Konstantinova IV.
Sistema Immuniteta v Ekstremal'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммунитета в Екстремальных Условиях Космическая Иммунология ***[The Immune System Under Extreme Conditions: Space Immunology]*** No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology].
Moscow: Nauka; 1988.
Pages 175-190.

Immunology, Cytology, Isolated Cells, Lymphocytes, Interferon, Concanavalin A; Cell Division, Cell Populations
Human Cells, Microbiology, Paramecia
Space Flight, Salyut-6, -7, COSMOS-1667

Abstract: This chapter is concerned with results of experiments exposing isolated human cells to weightlessness. Two groups of immunological studies of this sort have been performed on lymphocytes: the Interferon experiment performed jointly by Soviet and Hungarian scientists on Salyut-6, and a study investigating lymphocyte reactivity to ConA conducted by Swiss scientists.

The Interferon study had three parts: study of effects of space flight factors on production of interferon *in vivo* and *in vitro* and on the biological activities of various interferon-containing preparations. The second part involved investigation of isolated human lymphocytes exposed to weightlessness for production of interferon. The experiment was replicated twice, once in 1980 and the second time in 1981. A special device was designed with a metal body containing a rack with 10 teflon test tubes. Eight of these contained screw-on top compartments with internal volume of approximately 1 ml. At one end was a membrane separating the upper area from the main compartment and the other end attached to a screw top (Figure 38). The main compartment was filled with a suspension of blood lymphocytes, while the top compartment was filled with inductors of interferon formation. The two compartments were separated hermetically with a fixed membrane. Initially the screw of the upper compartment was not in contact with the membrane. When the screw was given 2-3 turns manually the membrane was pushed down into the main compartment and broke, allowing the liquids in the two compartments to mix. The two remaining test tubes, used for control purposes, merely lacked the upper compartment. A synchronous control condition was run on Earth.

In the first experiment, 7 hours before launch, 10 experimental and 10 control test tubes were filled on the ground with the same test material — a suspension of mononuclear cells from the blood of a healthy donor. In the second experiment tubes were filled 10 hours before launch. Inductors were placed in the top compartment. The flight material was transported along with the crew to Salyut-6. After docking, one of the crewmembers screwed down all the tops so that the membrane separating the two compartments broke and placed the tubes in a temperature control device at 37°. In the first experiment, the cells were left for 6 days, and in the second for 4. The cells' thermal chamber was switched off for 8 hours daily. Control cultures were treated analogously. The flight test tubes were returned to Earth by visiting crewmembers.

Inductors used (0.3 ml per compartment) in the first experiment were: polyinozine: polycytidylic acid — 600 μg; polyguanilic : polycytidylic acid - 600 μg; gossipol (a pigment derived from cotton) — 500 μg; a purified protein derivative of tuberculosis bacilli — 500 μg; and a Newcastle Disease Virus in a dose $10^7$ $LD_{50}$ per 1 ml. The NDV suspension underwent preliminary inactivation with ultraviolet radiation. The suspension from each test tube was centrifuged three hours after reentry. Activity of interferon in supernatants was measured using a test for the inhibition of the cytopathological effect of a Vesicular Stomatitis Virus in a

culture of fibroblasts of pulmonary tissue. For each measurement the culture was incubated with a standard preparation of interferon.

Viability of the cells after flight was similar in all eight experimental and two control test tubes, averaging 64%; the analogous value in the synchronous group was 70%. Tables 7 and 8 show that the suspension of human lymphocytes exposed on Salyut 6 for 7 days retained the capacity to synthesize interferon after contact with an inductor and even produced interferon more rapidly for all inductors (by a factor of 4-8 in experiment 1 and 2-4 in experiment 2) than cultures on the ground. Ground-based control studies ruled out the the possibility that these effects had causes other than weightlessness by: maintaining the lymphocytes and inductors for 7 days in a suspended state with constant agitation; increasing duration of contact with the inductor for 2 days; increasing area of cell surface in the suspension; holding the cells for 2 days after isolating them from donor blood.

Experiments by Swiss scientists on Spacelab-1 investigating the effects of space flight on the capacity of lymphocytes to react to ConA showed extreme depression of this function after space flight. This result was replicated on Spacelab-D1. Ground experiments with hypergravity showed enhanced reactivity of isolated human lymphocytes to ConA. Simulation of microgravity by clinostatting also depressed ConA reactivity.

A series of experiments were performed on Soviet space stations by French investigators (Planel and associates). These experiments used the unicellular organism *Paramecium aurelia.* A special device (Cytos) was developed to maintain the conditions needed for the paramecia to live and reproduce. Counting of the cells forming as a result of cell-division showed reliable activation of proliferation occurring on board Salyut-6. Estimate of rate of autogamy by assessing fragmentation of nuclei also showed stimulation of kinetics of proliferations associated with space flight. Flight cells were larger than control cells on hours 12, 24, 48, 60, and 96 after launch. However, cytochemical analysis showed that flight cells contained significantly less total protein than controls. There was also a decrease in the dry weight of flight cells. In flight cells, concentration of potassium, calcium, magnesium and phosphorus were elevated, while chlorine decreased insignificantly and sodium remained the same. Experiments performed on biosatellite COSMOS-1667 on *Infusoria* had analogous results — increase in rate of cell division and population growth. Factors other than weightlessness did not appear to be responsible for the effects. Possible mechanisms of the effect are increased nutritional value of the medium due to increased bacterial density or changes in energy metabolism due to "freeing up" of some energy that then could be used for reproduction. Another mechanism might be increased cell membrane permeability in weightlessness.

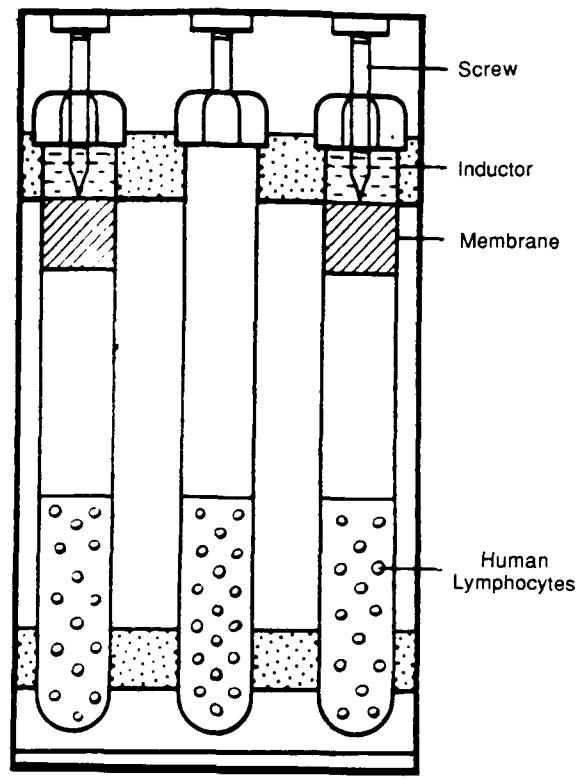



Figure 38: Diagram of the design of the "Interferon-1" device with compartments for interferon inductors and isolated human blood cells

Table 7: Induction of interferon by human lymphocytes on the ground and on the Salyut-6 space station (1980)

| Test Tube | Interferon Inductor | Dose μg | Interferon titer, ME | |
|---|---|---|---|---|
| | | | Earth | Salyut-6 |
| 1 | Polyin.-polycyt. acids | 600 | 40 | 320 |
| 2 | same | 600 | 40 | 320 |
| 3 | same | 600 | 40 | 320 |
| 4 | same | 600 | 40 | 320 |
| 5 | Gossipol | 500 | 20 | 80 |
| 6 | same | 500 | 20 | 80 |
| 7 | Tuberculosis bacilli | 500 | 40 | 320 |
| 8 | same | 500 | 40 | 320 |
| 9 | none | -- | 2 | 2 |
| 10 | none | -- | 2 | 2 |

Table 8: Induction of interferon by human lymphocytes on the ground and on Salyut-6 (1981)

| Test Tube | Interferon inductor | Dose μg | Interferon titer, ME | |
|---|---|---|---|---|
| | | | Earth | Salyut-6 |
| 1 | Polyin.-polycyt. acids | 600 | 80 | 312 |
| 2 | same | 600 | 80 | 312 |
| 3 | same | 600 | 80 | 312 |
| 4 | same | 600 | 80 | 312 |
| 5 | Newcastle virus | $10^7LD_{50}$ | 312 | 1248 |
| 6 | same | $10^7LD_{50}$ | 312 | 1248 |
| 7 | same | $10^7LD_{50}$ | 312 | 624 |
| 8 | same | $10^7LD_{50}$ | 312 | 624 |
| 9 | none | -- | 8 | 8 |
| 10 | none | -- | 8 | 8 |

**PAPERS:**

P1108(24/89) Vasilenko II, Shevel NM, SInyak YuYe.
***The use of hydrogen peroxide and lead oxide to remove urea from water.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 73-75; 1989.
[17 references; 2 in English]

Life Support Systems, Water Reclamation, Urea
Humans
Equipment and Instrumentation, Hydrogen Peroxide, Lead Oxide

Abstract: This paper cites the results of research on removing urea from water using hydrogen peroxides and oxide catalysts. These catalysts provide a high level of conversion of acetone and phenol into carbon dioxide at normal temperature and pressure. Purification was evaluated on the basis of difference between initial and final urea concentrations, measured photometrically and gasometrically. Initial concentrations of hydrogen peroxide were close to or greater than those needed for full oxidation of urea. Catalyst suspensions were kept for 30 minutes in a solution of urea, sampled for measurement of equilibrium, and then hydrogen peroxide was added to a concentration of 1.2-1.4 M and stirred. The solution was maintained at 20-24° C to prevent hydrolysis of urea. After gas emission had stopped for 30 minutes, the solution was poured off and analyzed and a new portion added to the catalyzer with the same initial concentration of urea. Precipitation of a yellow sediment when the emitted gas passed through baryta water indicated the formation of carbon dioxide.

In the absence of hydrogen peroxide, concentration of urea was determined only by its absorption on the surface of PbO. No further adsorption occurred when additional urea was added after the first portion. When hydrogen peroxide was added, the first portion of the solution was purified by 10.3%, and increased to 52% for subsequent portions. Increasing the amount of catalyst decreased of level of water purification. Obviously, adsorption of urea increases proportionately to the quantity of catalyst. However, increasing the rate of catalytic decomposition of hydrogen peroxide and deficit of oxidizer has a decisive effect on the water purification when PbO is increased. The slowing of the activation of large quantities of catalysts in repeated use is also related to the decreased time of contact between PbO and hydrogen peroxide and the slower modification of PbO. The authors conclude that it is possible in principle to use hydrogen peroxide and lead oxide to remove urea from water. To obtain a high rate of urea conversion, the optimum concentration of PbO must be maintained and there must be a significant excess of hydrogen peroxide.

Table: pH of the urea solution after contact with PbO

Figure 1: Decrease in concentration of urea due to adsorption and oxidation by hydrogen peroxide

Figure 2: The effect of number of uses of catalyst on purification of water

Figure 3: The effect of weight of PbO on the elimination of urea from water and rate of decomposition of hydrogen peroxide

P1109(24/89)*Zlotopol'skiy VM, Grishayenkov BG, Smirnov IA.
***Acceleration of formaldehyde synthesis as the first stage in production of carbohydrates from wastes.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 76; 1989.
[1 reference; 1 in English]

Life Support Systems, Carbohydrate Production, Wastes
Humans
Formaldehyde Synthesis

Abstract: Production of formaldehyde is a necessary step in the generation of carbohydrates from human waste products. An attempt to create a space life support systems based on an impulse arc plasmatron as a simulation of one of the processes of chemical evolution was not successful due to the need for low pressure and other conditions. Another possibility is the use of a barrier charge. An earlier attempt to accomplish this produced formaldehyde from carbon monoxide, but did so very slowly. Addition of methane as a catalyst accelerated the process. The current experiment attempted to further accelerate the process by combining a plasma and catalytic chamber in the same apparatus. The catalyst used was zinc oxide reduced in a hydrogen stream. Both the separate and the combined effects of the charge and catalyst were studied. When only the charge was used, an increase in gas flow rate led to lower transformation of initial gases into formaldehyde, probably due to insufficient time spent by the gases in the reaction space. When only the catalyst was used, the flow of gases had a weak influence on the formation of formaldehyde. When charge and catalyst were used together, formaldehyde formation was greater than the sum of that formed when the two treatments were applied separately. The increase due to combination increased as gas flow rate increased.

Table: Transformation (in %) of initial gases into formaldehyde after an hour of exposure in a circulating regimen

| Flow rate l/min | Charge | Catalyst | Combined effects |
|---|---|---|---|
| 0.60 | 5.45 | 4.21 | 10.53 |
| 1.25 | 2.47 | 4.32 | 11.10 |
| 4.00 | 1.98 | 4.83 | 15.06 |
| 6.35 | 0 | 5.07 | 16.13 |

P1117(24/89) Kondrachuk AV, Sirenko SP.
***Mathematical analysis of one conception of how the cupula of the semicircular canals functions.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3):90-23; 1989.
[10 references; 8 in English]

Mathematical Modeling
Humans
Neurophysiology; Semicircular Canals, Cupula

Abstract: The authors of this extended letter to the editor present a mathematical model of a new concept of cupula functioning, according to which the flow of endolymph in the subcupular space stimulates receptor cells while the cupula itself acts as a damper. Displacement of the cupula leads to decrease in the rate of endolymph flow in the ampulla and thus protects the hair cells from damage during high levels of angular acceleration. This concept is based on the following empirical data: 1) the area of a cross section of the ampulla is significantly greater than a cross section of the narrow portion of the semicircular canals, so that if the cupula is considered a transforming link, the threshold angle of deviation for the hair cells would be extremely small; 2) the structure of the canals is such that the flow of endolymph into the ampulla from the narrow portion is directed precisely at the bundles of hair receptors; 3) for stimulation in the physiological range, no discernible displacement of the cupula has been observed. The structural model developed represents the semicircular canals as a torus filled with incompressible Newtonian fluid (endolymph). The cross section of the torus is an elastic piston (cupula). Between the piston and the wall of the canal is a gap (subcupular space) filled with a fluid with viscosity equal to that of the endolymph. Within the gap are elastic spindles of cylindrical form (bundles of hair cells with density equal to that of the endolymph). This bundle is modeled as a rigid spindle firmly attached to the basal surface of the cell. Model parameters include the ratios of cross sections of the semicircular canals and hair cell bundles; endolymph density and kinematic viscosity; width of the gap and of the cupula. When inertial forces act on the system, endolymph begins to flow into the canal, the pressure of which causes the cupula to bend. The pressure differential causes fluid to flow into subcupular space in turn causing the hair cells to bend.

**PAPERS:**

P1120 (24/89) Yershikov SM.
***Rate of glyconeogenesis in the liver of rats in the recovery period after long-term hypokinesia.***
Voprosy Meditsinskoy Khimii.
35(3): 55-58; 1989.
[17 references; 3 in English]
Authors affiliation: Yaroslavl Medical Institute

Metabolism, Glyconeogenesis, Liver
Rats
Hypokinesia, Long-Term

Abstract: Experiments were performed on 60 white outbred rats, of which 32 formed the control group. The experimental group were confined in acrylic immobilization cages for 60 days and then transferred to common cages. Control animals were maintained under vivarium conditions. Animals were sacrificed at the end of the immobilization period and on days 1, 7, and 15 of recovery. Before sacrifice, animals received no food for 16-18 hours. Rate of glyconeogenesis was determined by incubating liver sections in Krebs-Ringer bicarbonate buffer and adding L-alanine, L-aspartic, L-glutaminic, α-ketoglutaric, pyruvic acid, or glycerine in a final concentration of 0.01 M. Incubation occurred in aerobic conditions at 40° C with constant shaking for an hour. Quantities of glucose in the incubation medium were measured using the glucooxidase method. Protein levels were also measured by an undescribed method. The concentration of glucose was measured in serum, while glycogen was measured in the liver.

The experimental treatment led to a significant decrease of glyconeogenesis in the liver, which was most evident when an alanine or pyruvate substrate was used and least evident when glutamate was used. Glycogen also declined sharply in the liver and blood serum. On the first day of recovery there was a moderate increase in glyconeogenesis in the liver on all substrates (compared to control group). Glycogen also increased from the last day of treatment, but was not above control level. The most extreme increase in glyconeogenesis in the liver was observed on day 7 of recovery on substrates of α-ketoglutarate, pyruvate, and glycerine, but not alanine or glutamate. Tissue glycogen was above control level. Serum glucose did not differ from control. On day 15 of recovery, glyconeogenesis dropped sharply in experimental animals and was substantially below control level. Glycogen decreased in the liver, and there was a tendency toward hypoglycemia. The reversal of changes occurring in early recovery are attributed to elimination of stress responses. The course of these changes should be considered when rehabilitation measures are developed.

Table: Formation of glucose from various substrates in liver sections of rats during 60 days of hypokinesia and the subsequent recovery period

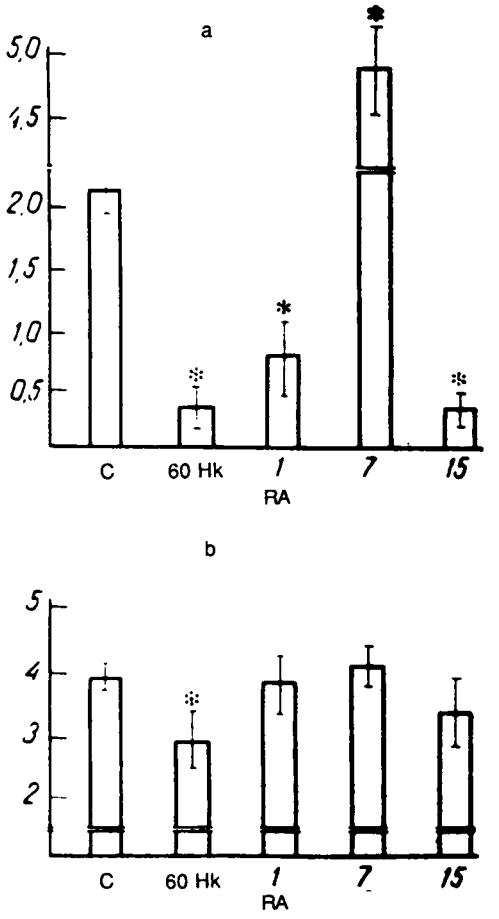



Figure: Concentration of glycogen (in g%) in liver tissue (a) and glucose (in mmole/l) in blood serum (b) in rats on day 60 of hypokinesia and during the readaptation period

* indicates statistically significant difference from control. Abscissa: C - control; 60 Hk - 60th day of hypokinesia; RA - readaptation period.

**PAPER:**

P1104(24/89)Polikarpov NA, Bragina MP.
***Sensitivity to antibiotics of opportunistic human indigenous microorganisms before and after isolation in an airtight environment.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 62-65; 1989.
[15 references; 3 in English]

Microbiology, Opportunistic Microorganisms, Drug Resistance
Humans
Isolation, Airtight Environment

Abstract: Fourteen individuals were studied, 8 of them before and after isolation in an airtight environment for from 96 to 175 days. Examinations were performed on days 30, 5, and 1 before the isolation and on days 1, 5, and 10 subsequent to it. A total of 800 cultures of opportunistic microorganisms were isolated, including *Klebsiella pneumoniae* 370 cultures, *Enterobacter aerogenes* 120, *E. cloacae* 40, *E. lyquefaciens* 10, and *Citrobacter freundii* 260. Bacteria were isolated from feces using a method developed by Bendig and Haenel. Identification of cultures as opportunistic followed Kalina and used W. Ewing's table and identification criteria. Bacterial sensitivity to drugs was determined through diffusion in agar using disks and the method of two serial dilutions in a dense medium. Data were processed statistically.

Analysis of the opportunistic microorganisms before treatment showed that they were resistant to 1-3 drugs (ampicillin, rifamycin [natural antibiotic produced by *Streptomyces meiterranei*], carbenicillin [Pyopen]). After 2 days in the sealed environment no changes were noted. However, after 6-8 and 96-175 days of treatment, 11 of the 14 subjects showed an increased number of antibiotic resistant forms of opportunistic microorganism. In a number of cases, microorganisms were isolated with resistance to 10-13 antibacterial drugs, and the majority of enterobacteria were resistant to 5-7 drugs. The authors conclude that isolation in an airtight environment extends the spectrum of resistance to antibacterial drugs in opportunistic enterobacteria isolated from subjects confined to hermetically sealed environments. The mechanism underlying this effect is conjectured to be individual changes in the composition of intestinal microflora, with certain species increasing and others decreasing in numbers.

Table: Comparative data on the spectrum of antibiotic resistance of opportunistic microflora in subjects examined

| Species of Enterobacteria | | | | |
|---|---|---|---|---|
| ***K. pneumoniae*** | ***E. arogenes*** | ***E. cloacae*** | ***C. freundii*** | **All species** |
| | | Before isolation | | |
| 3±0.19(180) | 3±0.15(60) | 3±0.12(20) | 3±0.22(140) | 3±0.22(400) |
| | | After isolation | | |
| 7±0.22(60) | 7±0.22(30) | 4±0.4(10) | 5±0.19(50) | 6±0.29(150) |

Numbers in parentheses refer to number of cultures studied.

**PAPERS:**

P1098(24/89) Konstantinova IV, Lesnyak AT, Bozhikov NV, Uchakin PN.
***Immunological mechanisms for regulating calcium metabolism in the bone tissue of humans undergoing long-term hypokinesia with head-down tilt (production of osteoclast-activating factor).***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 38-42; 1989.
[12 references; 5 in English]

Musculoskeletal System, Metabolism, Calcium Metabolism, Immunology, Osteoclast-Activating Factor
Humans
Hypokinesia with Head-Down Tilt, Long-Term

Abstract: This experiment tests the hypothesis that one of the mechanisms underlying loss of bone tissue on long-term space flights is associated with changes in the immune system, which can lead to local increase in the production of lymphokines and monokines, including osteoclast activating factor (OAF). Evidence confirming this hypothesis was previously obtained after a 120-day period of hypokinesia with head-down tilt. The present study subjected 10 healthy men to 370 days of head-down hypokinesia (angle not specified). Subjects were divided into two groups. The first received a series of countermeasures designed to prevent the adverse effects of the treatment. These included xydiphon (hydroxyethylidene biphosphonic acid), tocopherol, a protein-vitamin supplement, and exercise. The second group spent 120 days in bedrest after which prophylaxis was begun. A control group of men lived under normal conditions. Mononuclear cells were isolated from heparinized peripheral venous blood. To measure production of OAF, cells were cultured for 48 hours in a RPMI-1640 medium with bull serum albumin, HEPES-buffer and phytohemagglutinin. Activity of OAF in the supernatant was estimated by measuring capacity to reabsorb embryonal bone tissue of mice. Females on day 16 of pregnancy were injected with 40 μCu $^{45}Ca$; after a week the long tubular bones of the foreleg were extracted from the embryos, and after 24 hours of preincubation the bones were cultured for 48 hours in the presence of tested or controlled supernatants. The degree of resorption was estimated on the basis of emission of $^{45}Ca$ in the culture medium. The results were expressed in the form of a resorption index (IR), which was the ratio of emission of $^{45}Ca$ in the experimental culture to that in the control culture.

Total population of T-lymphocytes and subpopulations of "active" T-cells was measured in the blood of subjects using the method of spontaneous rosette-formation with sheep erythrocytes. Functional activity of T-lymphocytes was evaluated in a test with PHA on the basis of inclusion of $^{3}H$-thymidine in 48-hour cultures. Student's t was used to test data statistically. In 7 of the 8 subjects undergoing hypokinesia, resorption index was normal in the baseline period. In the first group of experimental subjects, the index of resorption (IR) was elevated on day 50 of treatment in 2 subjects, including the one with elevated initial level. On day 110 two more subjects showed elevated IR. IR was above the norm in 4 subjects on day 230 and in 5 on day 350. The pattern in group 2 was analogous After treatment IR normalized rapidly in the majority of subjects. Intergroup differences were not detected. No effects of treatment were detected in total population of T-lymphocytes, but concentration of "active" T-lymphocytes tended to be elevated throughout hypokinesia in both groups. Changes in PHA reactivity of T-lymphocytes did not occur during the first 7 months of treatment. However, this parameter subsequently decreased. Data is interpreted as supporting the hypothesis that immunological

mechanisms associated with OAF production contribute to calcium metabolism disorders in bones of humans undergoing long-term space flights.

Table 1: Capacity of mononuclear leukocytes of peripheral blood to produce OAF when activated by mitogen

Table 2: Amount of "active" T-lymphocytes in blood of subjects undergoing a 370-day period of hypokinesia with head-down tilt

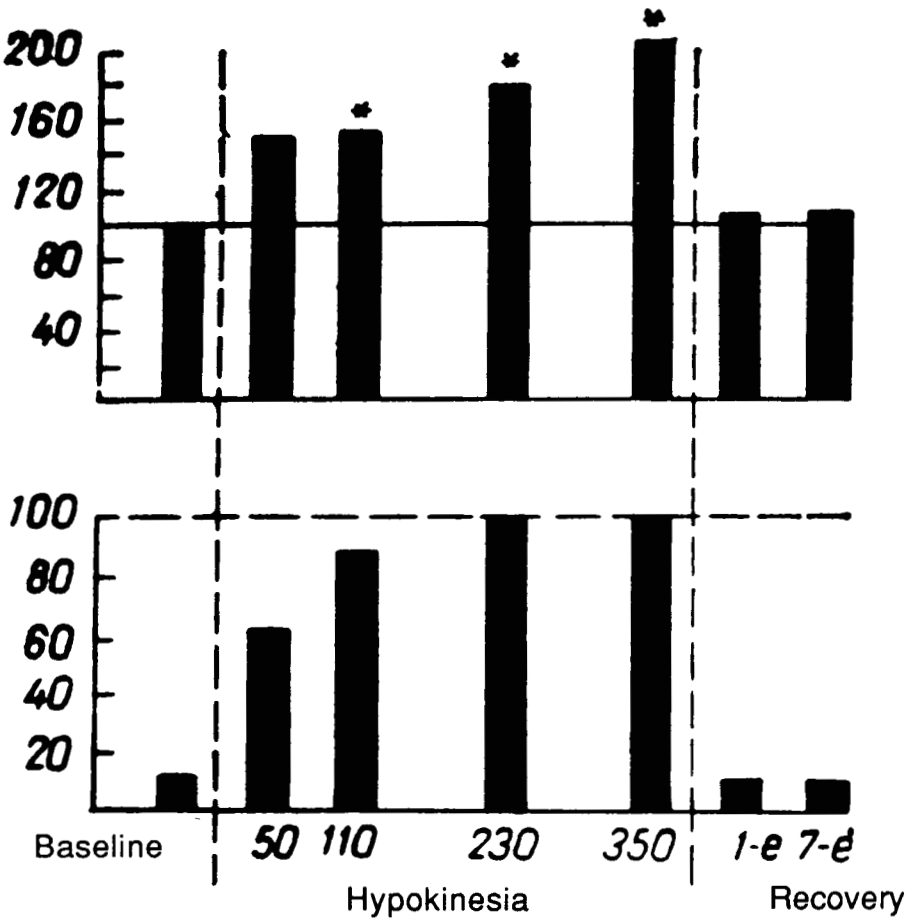



Figure: Production of OAF by human lymphocytes after varying periods of hypokinesia with head-down tilt (mean data for both groups)

Abscissa: duration of hypokinesia in days ; Ordinate - upper graph - IR (in % baseline); lower graph - number (in %) with elevated IR (>1.54). * $p < 0.05$

**PAPERS:**

P1101(24/89) Repin AA, Donskov AM.
***Physiological reactions to electrical stimulation of the labyrinths.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 49-53; 1989.
[14 references; 4 in English]

Physiological Response
Humans
Neurophysiology, Electrical Stimulation, Labyrinth

Abstract: Fifty-six individuals, aged 18-46, without apparent vestibular abnormalities or major health problems, were subjected to electrical stimulation of the projection of the labyrinth on the outer ear. Stimulation was transcutaneous, monopolar, and unilateral. Electrical conductivity was measured during testing in three zones (I - base of the helix; II - the area of the external acoustic meatus; III - area of the tragus of the external ear) with current of 20 μA. Cardiac parameters were recorded by EKG. Secretory and motor activity of the stomach was measured by intragastric pH-metry. Threshold somatotropic responses were estimated on the basis of eye movements, measured electrooculographically. Visual-vestibulomotor coordination was assessed by recording eye and head movements when the subject was required to fixate and shift his gaze. The labyrinth was stimulated with a generator producing electric current from 0 to 10,000 μA at frequency of 0 to 500 Hz. While the labyrinth was being stimulated, electrodermal, gastroduodenal, eye movement, and somatomotor reactions and changes in heart rhythm were recorded for each of five current ranges: 1 — from 0 to 20 μA.; 2 — from 40 to 100 μA.; 3 — from 100 to 300 μA.; 4 — from 400 to 1200 μA.; 5 — from 1300 to 1800 μA. All of these were in a frequency range of from 0.2 - 0.5 Hz. The duration of the entire study was not less than 10 min.

In zone I response to monopolar unilateral stimulation by electric current of 40 - 100 μA. depended on polarity. In cathode stimulation, changes in stomach motor function and heart rhythm occurred in 12-36 seconds. Secretory response occurred later (minutes 3-5). Acid formation was inhibited, while stomach tonus increased. There was a tendency toward tachycardia, and skin electroconductivity increased. Discomfort was noted. When the anode was applied, effects were exactly opposite. When the stimulating current was moved to zone III, responses were less pronounced (not statistically significant), but still dependent on polarity. When current was increased above 100 μA, local pain was note, complicating determination of visceral reactions. A two-phase eye movement occurred in response to cathode stimulation at a current of 920±200 μA. In the first phase there was a ipsilateral phase deviation of the eyes of amplitude 4-6° and duration of 20-40 msec. The second phase involved a contralateral tonic aversion of the eyes no less than 900-1300 msec in duration with amplitude 10-12°. Change in stimulation polarity led to an inversion of the eye movement response. Gaze fixation was disrupted in a way that depended on polarity of stimulation. Coordination of eye and head movements was also disrupted. At the same time, gaze tended to drift, giving rise to the sensation that objects were moving. Increase of current to 1300-1880 μA. led to amplitude asymmetry of eye movements and head turning, ipsilateral hypermetry, and contralateral hypometry. These changes were accompanied by sensations of dizziness, discomfort, and marked changes in fixation. Changes in heart rhythm and motor function of the stomach occurred only after 10 minutes of stimulation. No marked changes in secretory functions were observed.

Table: Changes in autonomic parameters in response to electric transdermal stimulation of the projection of the labyrinths on the external ear

P1106(24/89) Telezhnikov AV, Savchuk LA.
***Autocorrelational analysis of electronystagmograms.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 68-71; 1989.
[8 references; none in English]

Neurophysiology, Rotational Nystagmus
Humans, Patients, Cochleovestibular Disorders
Autocorrelational Analysis

Abstract: Electronystagmograms of rotational nystagmus were recorded for 30 healthy subjects (20 males, 10 females) with normal vestibular function and 30 patients suffering from cochleovestibular disorders. The 0 - 50 Hz frequency range was selected for analysis. When nystagmic parameters were analyzed using traditional methods, healthy individuals and patients could not be distinguished. When nystagmic parameters occurring in different time intervals were autocorrelated, however, significant differences were found. In normal subjects, the Yastremskiy coefficient (seemingly the rate of decrease of autocorrelation as time lag increases) was relatively constant and was not a function of time lag, but in vestibular patients the Yastremskiy coefficient was a function of time lag. In normal subjects nystagmus induced by rightward and leftward rotation were positively correlated, exceeding correlations for subjects with vestibular disturbance. In these patients, negative autocorrelations were noted between right and left nystagmic parameters. The authors conclude that sample autocorrelations of nystagmogram parameters may be used as diagnostic indicators.

Table: Evaluation of sample autocorrelations in healthy subjects and patients with cochleovestibular impairments

Figure 1: Graphs of Yastremskiy coefficient and sample autocorrelation functions of rotational nystagmus in a healthy subject and patients with cochleovestibular disorders

Figure 2: Flow chart of autocorrelational analysis of electronystagmograms

P1112(24/89)* Gavrilin VK.
***Comparison of two methods for assessing the paired activity of the human otolith apparatus.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 82-83;1989.
[13 references; in English]

Neurophysiology, Otolith, Paired Activity
Humans
Methods of Assessment, Afterimage, Compensatory Eye Movements

Abstract: Paired activity of the otolith apparatus was measured using two methods. The first method involved measuring parameters of the ocular counterrotation reflex of an afterimage. A subject was exposed to a flash of light and then shifted from the vertical to horizontal position first on his left and then his right side. The angle of incidence of the afterimage was measured on each side, and otolith asymmetry was identified as the difference between their mean values. The second method involved recording the otolith compensatory eye movements using electrooculography in response to graded exposure to linear acceleration on parallel swings alternating in direction. Mean amplitudes of vertical compensatory movements of the right and left eyes and horizontal binocular compensatory movements were recorded while subject lay on his back, and on his right and left sides. Asymmetry was defined as the difference between the mean values for the right eye with subject on his right side and for the left eye on the left side. A total of 100 healthy males were used as subjects using the first method, and 51 using the second.

Using the asymmetry measure derived from ocular counterrolling, a total of 41% of subjects were identified as displaying asymmetry (more than 6° difference); asymmetry was equally likely in either direction. Using the compensatory eye movement measure, 38% of the subjects were identified as displaying asymmetry (more than 7° difference). Of these, 17 out of 19 showed greater compensatory movement on the left side. In 49 subjects, correlational analyses were performed between the measures of asymmetry obtained using the two methods. Mean correlation was +0.403. The author recommends the use of both methods to complement each other in studies of paired otolith functioning in response to various types of stimulation.

P1113(24/89)* Bodo G, Elkan K, Bentse G (Hungary).
***The effect of the drug "Yumex" on the development of experimental motion sickness.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 84; 1989.
[4 references; 1 in English]

Neurophysiology, Motion Sickness, Experimental
Humans
Countermeasures, Drugs, Deprenyl, Dramamine

Abstract: In their search for a drug that protects against motion sickness but does not induce drowsiness and impairment of cognitive functioning, the authors selected deprenyl (chemical name unknown; trade name Yumex). This drug selectively depresses monoamine oxidase (MAO-B), leading to an increase in neuronal dopamine. The experiment evaluated the effect of Yumex, dramamine, and a placebo in 3 groups, each containing 11 volunteers. Motion sickness was induced by an unspecified method. Initial vestibuloautonomic resistance was identified with time elapsed between beginning of treatment and development of marked nausea. Three days after baseline studies, subjects in group 1 were given one dose of Yumex (four tablets); those in group 2 received one dose of 100 mg dramamine, and group 3 received a placebo. Two hours after ingestion of drugs the subjects were again subjected to vestibular stimulation. They were then given an attention test used in aviation medicine.

Yumex significantly delayed the development of motion sickness symptoms; the effect of dramamine was somewhat greater. No effects of Yumex were noted on the attention test. However, subjects receiving dramamine noted sensations of drowsiness and fatigue; those receiving Yumex did not. The use of Yumex is recommended.

Figure: The effect of Yumex, dramamine, and a placebo on autonomic resistance of subjects.

P1118(24/89) Gorgiladze GI, Bryanov II.
***Space motion sickness.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 4-14; 1989.
[82 references; 33 in English]

Neurophysiology, Space Motion Sickness
Humans, Cosmonauts
Review Article

Abstract: This review article describes the phenomenology of the space motion sickness noted in 80-93% of cosmonauts during space flight and after reentry, especially after long-term flights. The similarity of their symptoms to ground-based motion sickness has led to the belief that this ailment is vestibulosensory and vestibuloautonomic in nature. This idea is confirmed by clear evidence of changes in vestibular function during space flight and upon return to Earth. The authors discuss a number of theories of the ontogeny of space motion sickness.

The sensory conflict or mismatch theory is perhaps the most common and attributes space motion sickness to the mismatch among sensory inputs supporting spatial perception. Sensory conflicts may be intralabyrinthine with a lack of agreement among signals entering the central nervous system from different vestibular receptors, or intersensory, when contradictory signals reach the central nervous system from the labyrinth and other spatial receptors (visual, tactile, kinesthetic, etc.). Both types of conflict involve the distortion of an expected signal from receptors sensitive to gravity, which fails to reinforce information on motion coming from visual input and semicircular receptors. This theory is based on the psychophysiological idea that the central nervous system constructs a neural model of a stimulus. During adaptation to weightlessness, a new neural stimulus model is constructed, which is adapted to the new sensory pattern and supports appropriate functioning under the new conditions. One way to facilitate adaptation is through decreasing the role of gravity receptors in control and perception of body movements. That this occurs is confirmed by the fact that threshold of perception of linear acceleration is diminished in weightlessness. A second mechanism is recoding or reinterpretation of otolith signals in the central nervous system, a process involving modification of vestibulo-eye movement and vestibulospinal reactions, and canal otolith interactions. Finally, dominance of visual information in maintaining body position in space increases. Given adaptation to space conditions, return to Earth involves an analogous sensory conflict. The authors criticize this theory on the grounds of the lack of clarity in the notion of conflicting signals and the mechanism through which they are formed and lead to neural activity.

A new variant of this theory refers to conflict between sensory experience and long-term memory. This second theory involves disruption of paired functioning of the labyrinths, This theory is based primarily on data from clinical physiological examination of cosmonauts, and postulates that inequality of bioelectric activity in the vestibular nuclei of both sides (occurring naturally on Earth) is compensated for by the central nervous system. Since asymmetry is due to differences in weight, original differences would be altered in space and the original compensation would no longer be appropriate. From clinical practice it is clear that asymmetry does give rise to vestibular symptoms and/or lack of resistance to motion sickness.

The third theory involves the circulation of blood and cerebrospinal fluids and attributes space motion sickness to the cephalad redistribution of body fluids and the disappearance of the hydrostatic gradient. Symptoms of this phenomenon (e.g., facial edema) occur during the first few hours of space flight and gradually disappear by days 3-7. Impedance plethysmography in space has confirmed the existence of a whole series of fluid shifts. It has been found that countermeasures used in space to prevent blood pooling in the upper body attenuate or eliminate

symptoms of motion sickness. The mechanism postulated in this theory is as follows. Increased venous and cerebrospinal pressure induced by cephalad fluid shifts lead to change in pressure of intralabyrinth fluids or have an indirect effect on blood circulation in the labyrinth due to the lack of a mechanism of autoregulation. This in turn leads to change in the pattern of spontaneous and evoked afferent impulses from the receptors of the labyrinths, resulting in vestibular dysfunction with symptoms of motion sickness. In addition, it is possible that fluid shifts in weightlessness alter angiotensin activity, causing an imbalance in the neurotransmitter chain of neurons in the chemoreceptor trigger zone of the medulla, altering the functional state of the emetic center and causing the symptoms. Head-down tilt simulating fluid shifts in weightlessness produces symptoms analogous to motion sickness in some but not all subjects. Other vestibular symptoms associated with the head-down position include changes in vestibular threshold, spontaneous and positional nystagmus, changes in the otolith reflex, asymmetry and error in determining spatial coordinates, illusions associated with head movements, and intensified response to caloric irrigation.

It is argued that the failure of selection tests to eliminate candidates prone to space motion sickness, together with the failure of intensive cosmonaut training to prevent the condition is due to insufficient similarity between the ground-based motion sickness inducers and the phenomena occurring in space. Promising countermeasures currently being tested include: prismatic glasses proven useful for simulating sensory conflict; "prophylactic adaptive training" in which head movements are accompanied by shifts in visual representations of objects; evaluation of initial vestibular asymmetry; evaluation of changes in the spinal H-reflex when the otolith apparatus is stimulated; determination of an individual's autonomic status; active movements of the head in parabolic flight; training of the visual system to improve the fixating capacity of the eyes; drugs increasing adaptive capacities; electrical stimulation of both labyrinths during water immersion; autogenic training and biofeedback; voluntary muscle exercises combined with electric stimulation; application of electric current to the brain; special devices for creating excess pressure on the soles of the feet; creation of tension on the cervical portion of the spinal cord and occipitocervical antigravity muscles; and measures to prevent pooling of fluids in the upper body.

The authors conclude that none of the individual theories can by itself explain the entire range of phenomena associated with space motion sickness. However, these theories are not inimical, but more likely are interrelated and complementary. Each postulated cause may participate in the genesis of space motion sickness. Either may predominate in a particular individual.

P11121 (24/89) Atchabarov BA, Abeuov BA, Sydykov US.
***The effect of head-down position on resorption of cerebrospinal fluid and certain hemodynamic parameters during elevated intracranial pressure.***
Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya.
1989(1): 23-26.
[8 references; 1 in English]
Authors' Affiliation: Institute of Pathology, Kazakh Ministry of Health

Neurophysiology, Resorption of Cerebrospinal Fluid
Dogs
Head-Down Position, Elevated Intracranial Pressure

Abstract: This experiment studied the interrelationship between circulation of blood and cerebrospinal fluid in a head-down position with elevated intracranial pressure. Experiments were performed on 14 outbred dogs under anesthesia. Graded increases in intracranial pressure were induced using a hydrostatic column with artificial cerebrospinal fluid attached with a puncture needle to the cistern of the great vein of the ambient cistern. Rate of resorption of cerebrospinal fluid as the level of pressure increased was measured on the basis of consumption of the artificial fluid. The baseline rate of production and resorption of cerebrospinal fluid was assumed to be a constant. Resistance to resorption — a parameter indicative of drainage in the cerebrospinal fluid tract was computed using two formulae. Absorption $resistance_1$ = intracranial pressure/rate of resorption of cerebrospinal fluid; Absorption $resistance_2$ = (intracranial pressure - pressure in venous sinuses)/rate of resorption of cerebrospinal fluid. Parameters measured continuously included intracranial pressure, pressure in the venous sinuses, arterial pressure in the carotid artery, venous pressure in the jugular vein, and respiration rate. Extremely sensitive gauges made it possible to record true pressure. Body position was changed through the use of a special rotation stand. Control parameters were obtained from the same animals in a horizontal position.

Shifting the animals into head-down position increased intracranial pressure, pressure in the sinuses, arterial and venous pressure, and also increased respiration rate. The most extreme shifts occurred during the first few minutes after position shift. After 10 minutes parameters had dropped somewhat, but remained substantially above control level. Graded artificial elevation in intracranial pressure had different effects on hemodynamics depending on body position. In horizontal subjects, increase of intracranial pressure to 800 mm $H_2O$ induced no changes in arterial or venous pressure. Pressure in the sinuses changed parabolically, with a plateau starting with intracranial pressure of 600-700 mm $H_2O$. In head-down position, elevating intracranial pressure increased systemic arterial and venous blood pressure as well as pressure in the sinuses. Arterial pressure increased with each increase in intracranial pressure, while venous blood pressure increased initially and then stabilized. Pressure in the sinuses was analogous to that in horizontal position. It is argued that the changes noted in venous pressure were due solely to the head-down position, while changes in arterial pressure were due to both factors. For a given level of intracranial pressure, rate of resorption of cerebrospinal fluid was lower in head-down than in horizontal position. Thus, resistance to absorption ($RA_1$) was higher than in the horizontal position.

The authors argue that changes in resorption of cerebrospinal fluid in head-down position were induced primarily by increased level of pressure in the sinus leading to decreased pressure gradient between the cerebrospinal fluid and the venous bed, where outflow of cerebrospinal fluid occurs. However, decrease in outflow rate may also be affected by another factor, since the parameters of resorption resistance in head-down position are somewhat higher than in horizontal position. It is possible that this is associated with increased production of cerebrospinal fluid. Some data suggest that the level of intracranial pressure has little effect

on the formation of cerebrospinal fluid; thus the major factor changing the production of cerebrospinal fluid in head-down position would be change in cerebral blood circulation.

Figure 1: Change in intracranial pressure, pressure in the sinuses, arterial and venous blood pressure, and respiration rate when animals are placed in a head-down position

Figure 2: Change in arterial pressure, pressure in the sinuses, and venous pressure in response to graded increases in intracranial pressure in animals in head-down and horizontal position

Figure 3: Change in resistance to resorption in horizontal and head-down positions

P1122(24/89) Leshchinyuk II, Konovalova YeO, Kvitchataya AI, Shamray
***The effect of antimotion sickness drugs (vestibuloprotectors) on the cyclic nucleotide system in experimental motion sickness.***
Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya.
1989(1): 26-28.
[13 references; 4 in English]
Authors' Affiliation: Ukrainian School of Medicine, Kharkov

Neurophysiology, Motion Sickness, Experimental, Cyclic Nucleotides
Rats
Countermeasures, Drugs, Antimotion-Sickness

Abstract: The authors studied the effects of alkyl derivatives of 2-mercaptobenzymidazol (belonging to a class the Soviets call actoprotectors because they are purported to stimulate work capacity). The objective here was to study the effects of two of these drugs, bemityl and etoxybemithyl, earlier shown to depress motion sickness, on changes in levels of cAMP and cGMP during a motion-sickness-inducing procedure. Subjects were 104 Wistar rats, rotated in the horizontal plane with angular velocity of 18 degree/seconds. Drugs were administered intraperitoneally in water solutions. The animals were divided into 8 groups. Group 1 was the control; group 2 was exposed to rotation alone; group 3 received bemityl in a dose of 50 mg/kg; group 4 were given bemityl in a dose of 100 mg/kg; group 5 received bemytyl in a dose of 200 mg/kg; group 6 received etoxybemityl in a dose of 50 mg/kg; group 7 received etoxybemityl in a dose of 100 mg/kg; and group 8 received 200 mg/kg of etoxybemityl. All animals were rotated 60 minutes after administration of drugs. and were were sacrificed immediately after rotation. Levels of cyclic nucleotides were measured in blood plasma using radioimmunological kits.

Animals exposed to motion-sickness-inducing procedures displayed levels of plasma cAMP 2.5 times that of controls, while cGMP was lower. Bemityl in the a dose of 5 mg/kg diminished the increase in cAMP but did not prevent it, and increasing dose to 100 and 200 mg/kg did not enhance the drug's effects. A dose of 50 mg/kg etoxybemityl performed even better than an equivalent dose of bemityl in inhibiting cAMP rise, but did not normalize the parameters. Doses of 100 and 200 mg/kg etoxybemityl prevented plasma cAMP from exceeding control after rotation. Doses of 50 mg/kg of either drug prevented plasma cGMP from decreasing. However, doses of 100 and 200 mg/kg of both preparations were associated with cGMP levels as low as after rotation alone.

The authors interpret their data as suggesting that the effects of the drugs are mediated through by cyclic nucleotides. It is assumed that changes in plasma cAMP are accompanied by changes in this substance in the brain.

Table: Change in levels of cyclic nucleotides in blood plasma of rats in response to rotation and administration of motion sickness drugs

P1093(24/89) Krasnov IB, Olenev SN, Babichenko II, Kesarev VS.
***Morphological and histochemical analysis of the brain.***
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 97-104.

Neurophysiology, Brain Morphology, Brain Histochemistry
Developmental Biology, Rats, Fetuses, Neonates
Space Flight, COSMOS-1514

Abstract: The brains of 18-day-old fetuses and 15-, 30-, and 100-day-old rats developing in weightlessness and analogous material from synchronous and vivarium control groups underwent morphological and histochemical analyses. The material was fixed using Lilly's method in a mixture of 100-degree ethanol, frozen acetic acid and 40% formaldehyde (85:5:10), and then poured into paraffin. Frontal sections 10 μm thick were stained with hallocyanine-chrome alums.

Sections 15 μm thick of the hindbrain of 18-day-old fetuses, frozen in liquid nitrogen. were prepared in a cryostat and histological methods were used to determine the activity of alkaline phosphatase, (AlP), acid phosphatases (AP), acetylcholine esterases (ACE), monoamine oxidases (MAO), succinate dehydrogenases (SDH), lactate dehydrogenases (LDH), and NAD-$H_2$- and NADPH-$H_2$-diaphorase. Rates of histochemical reactions for determining activity of LDH and SDH were measured using the two-wave method with a cytophotometer.

Morphometric analysis of cytoarchitectonics of the neocortex in 18-day-old fetuses was performed using a teleanalyzer. In all areas of the cortical plate, the thickness of the wall of the hemisphere and its layers were measured in five locations in every fifth frontal section stained with hallocyanin.

For electron microscopic studies, the hypothalamus and hypophysis were fixed in a 2.4% solution of glutaric aldehyde, prepared in a phosphate buffer (0.08 M for the brain of fetuses and neonates, 0.1 M for animals of the older age groups; pH 7.2), and then in a 2% solution of osmium tetroxide in the same buffer, after which it was poured in araldite. Ultrathin sections were studied.

Macroscopic study of the brains of 18-day old fetuses and 15-, 30- and 100-day-old rats that had developed prenatally in space revealed no pathological changes differing from control groups.

Optical microscopy of the frontal section of the brains of 18-day-old fetuses of the experimental and control groups showed a well defined cortical plate in the cerebral hemispheres that represent a layer of neuroblasts beginning to stratify. The so-called "migration paths" of cells along the fibers, growing from the tubercle of thalamus into the cerebral cortex, were well-defined. Periventricularly, in the zone of the medullablast matrix, there were numerous mitoses occurring in the inside of the hemisphere and striatum. The level of mitotic activity of the neuroblasts and glial elements in this area of the brain was no different in 18-day-old fetuses of the flight group and control animals. The striatum was formed of very densely packed and relatively undifferentiated cells. The cerebellum was represented by the rudiments of the cerebellar plate with diffusely distributed and relatively undifferentiated cells. Measurement of the size of the earliest nerve cells of the brain to differentiate — the neurons of the nucleus of the trigeminal nerve — revealed no statistically reliable differences between the experimental and control animals.

Measurement of the number of capillaries in the striatum of the brain in flight fetuses revealed a 40% and 59% increase in their quantity in a unit area compared to the vivarium and ground-based synchronous control groups, respectively.

Histochemical study of activity of enzymes in tissue of the hindbrain of 18-day-old fetuses of the control groups revealed ACE activity in the cells of the reticular formation, in the nerve fibers in the cervical zone, at the bottom of the third ventricle, in nuclei of pairs VII, X and XII of the cranial nerves and in the descending nucleus of the trigeminal nerve. Activity of MAO in the structures of the hindbrain is still low at this developmental stage. Somewhat greater MAO activity was observed in the cervical area. AP activity was distributed diffusely throughout the structures of the hindbrain and was high only in the area ventral to the bottom of the third ventricle. AIP activity was mainly concentrated in the endothelium of the capillaries of the brain; in nerve tissue this activity was insignificant and diffuse. Activity of NAD-$N_2$-diaphorase was rather high in all structures of the hindbrain, somewhat higher than the activity of this enzyme in the cervical zone and the nucleus of the facial nerve and descending nucleus of the trigeminal nerve. Distribution of NADP-$H_2$-diaphorase activity in the structures of the hindbrain was analogous to the localization of NAD-$H_2$-diaphorases, but the level of its activity was lower. The activity of LDH was very high and diffusely distributed in the hindbrain, while activity of SDH was still very low. The level and distribution of NAD-$H_2$- and NADP-$H_2$-diaphorases, MAO, ACE, SDH, AP, and LDH in the hindbrain of 18-day-old fetuses of the flight group did not differ from the corresponding parameters in the control groups. Activity of AIP in the hindbrain of flight fetuses was distributed similarly to that in the control, although visual evaluation revealed the level of AIP activity in the endothelium of the capillaries to be somewhat lower than in the vivarium and synchronous control groups, while cytophotometry showed AIP activity to be higher in nerve tissue for the flight group.

Qualitative analysis of the cytoarchitechtonics in the cerebral neocortex of 18-day-old fetuses revealed no differences in the degree of structural differentiation in the experimental and control groups. Quantitative analysis of the architectronics of the same structures, presented in Table 31, revealed a tendency for the width of the matrix to be greater and the width of the cortical plate to be lower in fetuses of the flight and ground-based synchronous groups than in the vivarium animals.

Electron microscopic analysis of the structures of the hypothalamus established that by day 18 of prenatal development, the ultrastructure of the neurosecretory neurons and the neuropile of the supraoptic nucleus of the hypothalamus were relatively fully formed in fetuses of the vivarium and synchronous control groups (Figure 36). The nuclei of the neurons, characterized by high density of nuclear chromatin, had a narrow perinuclear space. The cytoplasm contained many polyribosomes and mitochondria with pronounced cristae; well-developed canaliculi of the granular endoplasmic reticulum. Elements of the Golgi complex had the appearance of two or three flat cisternae, surrounded by many small vesicles, among which were neurosecretory granules. In the synchronous control group, the neurosecretory cells had a higher density of nuclear chromatin and canaliculi of the granular endoplasmic reticulum compared to the vivarium control. The neuropile of the supraoptic nuclei had the form of fine unmyelinated fibers and dendrites with well-defined microtubules and mitochondria, dendritic and axonal growth envelopes, and also dendritic and axonal terminals, which were full of synaptic vesicles.

The neurosecretory granules of the flight group fetuses (Figure 36) showed elevated density and area of distribution of the nuclear heterochromatin compared to both control groups, widening of the perinuclear space, and decreased number of polyribosomes and canaliculi of the granular endoplasmic reticulum in the cytoplasm. The reticulated Golgi apparatus was represented only by isolated large vesicles. The neuropile contained virtually no fine dendritic or axonal

terminals with synaptic vesicles. The growth envelopes showed deformations and adhesions of large vesicles, and damage and thickening of the mitochondria. In the unmyelinated fibers, widening of the microtubules could be observed.

In the median eminence of 18-day-old fetuses in the control group the neuropile was composed of fine unmyelinated axons with the microtubules retained and a large number of growth envelopes that contained large vesicles, two or three neurosecretory granules, and mitochondria with a dense matrix and pronounced cristae. In the neuropile of the median eminence of flight fetuses, the unmyelinated fibers and growth envelopes of axons and dendrites had undergone changes similar to those occurring in the neuropile of the supraoptic nuclei described above.

Neonate flight rats had developed all the major elements of the ultrastructure of neurosecretory cells characteristic of the analogous neurons of neonate rats of the vivarium and synchronous control groups (Figure 37). However, compared to the neurosecretory neurons of rats in the vivarium condition the nuclei of these cells in flight rats showed elevation of chromatin density and an increased number of Golgi apparatus elements, microvesicles and neurosecretory granules in the cytoplasm. In the neurons of the supraoptic nuclei of neonate rats in the synchronous control group, there was a very pronounced widening of the canaliculi of the granular endoplasmic reticulum and the cisterns of the Golgi apparatus, lightening of the mitochondrial matrix, and significant decrease in the number of neurosecretory granules compared to the animals in the vivarium and flight groups.

In the axonal terminals of the median eminence in the posterior lobe of the hypophysis of neonate flight group rats (Figure 37) there was an increase in the quantity of neurosecretory granules, the majority of which were granular, and also a sharp increase in the number of light microvesicles 40-60 nm in diameter grouped in the central portion of the terminals. The axonal terminals of the median eminence in rats of the synchronous control group were poor in neurosecretory granules and light microvesicles 40-60 nm in diameter.

Pituicytes of neonate rats of the flight and synchronous control groups displayed hypertrophy and vesiculation of the elements of the Golgi apparatus compared with the vivarium control, and increased numbers of canaliculi in the granular endoplasmic reticulum and free ribosomes, lightening of the mitochondrial matrix, and pronounced condensation of chromatin in the nuclear envelope (cf. Figure 37).

By day 15 of their lives, the ultrastructure of neurosecretory cells in the supraoptical nuclei were well formed in rats of the vivarium control group. The nuclei displayed homogeneous distribution of chromatin. The perinuclear space was narrow. In the perikaryon, the elements of the granular endoplasmic reticulum took the form of narrow branching canaliculi, with the ribosomes on the outer surface of the membrane. A large number of free ribosomes in the form of polyribosomes were also localized in the cytoplasm. Elements of the Golgi apparatus took the form of three or four flat cisternae, surrounded by electron transparent microvesicles and large, 120-170 nm in diameter, neurosecretory granules with electron dense centers. The mitochondria had well-defined cristae. The axonal terminals of the neurosecretory cells in the median eminence and posterior lobe of the pituitary contained synaptic vesicles 40-60 nm in diameter and 1-2 vesicles up to 180 nm in diameter, aside from neurosecretory granules with a well-defined electron-dense center.

The ultrastructure of neurosecretory neurons and their axonal terminals in the medial eminence and posterior lobes of the hypophysis in 15-day-old rats of the flight and synchronous groups did not differ from the corresponding parameters in animals of the vivarium control.

By day 30 of the rats' lives there were no differences in the ultrastructure of neurosecretory cells of the supraoptic nuclei, their axons and terminals in the medial eminence and posterior lobe of the hypophysis from day 15. No differences were found between experimental and control animals.

Thus, macroscopic and visual light microscopic studies of the brains of 18-day-old fetuses and then of 15-, 30-, and 60-day-old rats spending a portion of their prenatal period in space, did not reveal any changes in the development of brain structures up to day 100 of postnatal development.

The level of activity and distribution of activity of key enzymes of catabolic (LDH, SDH, NA DP-$H_2$, and NAD-$H_2$-diaphorase) and mediator metabolism (MAO and ACE) in the tissue of the brain of 18-day-old flight fetuses remained unaltered, suggesting normal establishment of catabolic and mediator metabolism of substances in the brain of fetuses during prenatal exposure to space.

At the same time, the development of rats under space flight conditions was evidently accompanied by a decrease in the activity of AlP in the endothelium of the capillaries and increased activity of this enzyme in nerve tissue of the hindbrain of 18-day-old flight fetuses. Increase in the number of capillaries observed in the brain striatum of 18-day-old fetuses developing in space, evidently compensatory in nature, was another sign of some deficiency in brain oxygenation in the flight fetuses. A possible reason for insufficient oxygenation of the brain may be the decreased size and weight of the placenta observed in the pregnant flight rats

The fetuses that had developed under space flight conditions showed a tendency for delay in the process of migration of cellular elements of the neocortex from the matrix to the cortical plate, and a decrease in the thickness of the cortical plate in the wall of the cerebral hemispheres in 18-day-old flight fetuses. However the presence of an analogous tendency in the brains of rat fetuses of the ground-based synchronous group implied that the reason for this was not exclusively weightlessness.

Morphological study of brain structures receiving neural impulses from the otolith apparatus — the cerebellar nodulus and the lateral vestibular nucleus — showed that in 18-day-old rat fetuses the nodulus of the vermis is still not formed, since the formation of the sulci separating the nodulus from the remainder of the vermis occurs on day 19 of prenatal development, while the cells of the lateral vestibular nucleus complete their differentiation by day 13 of prenatal ontogeny. And although type I and II hair cells in the utricular modulus of rat fetuses complete their differentiation on days 14 and 15 of prenatal ontogeny, respectively, the formation of synaptic contacts between nerve fibers and these cells, and thus the capacity to transmit impulses from the otolith apparatus to the brain occurs only on day 18 of embryonal development, i.e., after the mothers had returned to normal gravity. It is possible that this explains the absence of morphological changes in the lateral vestibular nucleus, which receives impulses from the otolith apparatus of flight fetuses.

The state of the ultrastructure of neurosecretory cells and neuropiles in the supraoptic nuclei of the hypothalamus, and also the ultrastructure of the axons and terminals of these cells in the medial eminence in 18-day-old fetuses developing in weightlessness suggests some delay in differentiation of neurosecretory cells during the neuroblast developmental stage as well as in development of changes in the microtubules of the unmyelinated nerve fibers and in the growth cones of axons and dendrites. It cannot now be determined whether retardation in differentiation of nerve cells is a direct result of exposure of the cell to weightlessness.

Table 31: Width (μm) of layers of the walls of the cerebral hemispheres of the brains of 18-day-old rat fetuses

| Group | Boundary zone | Cortical layer | Substantia ntermedia | Matrix | Wall of the hemisphere |
|---|---|---|---|---|---|
| F | 22.7±2.1 | 100.2±10.4 | 117.4±15.6 | 114.4±10.9 | 354.7±35.3 |
| SC | 27.5±1.2 | 118.1±7.6 | 131.8±15.4 | 142.4±10.4 | 419.8±25.5 |
| VC | 23.0±3.2 | 115.3±21.6 | 125.2±21.1 | 88.9±9.2 | 352.4±48.1 |

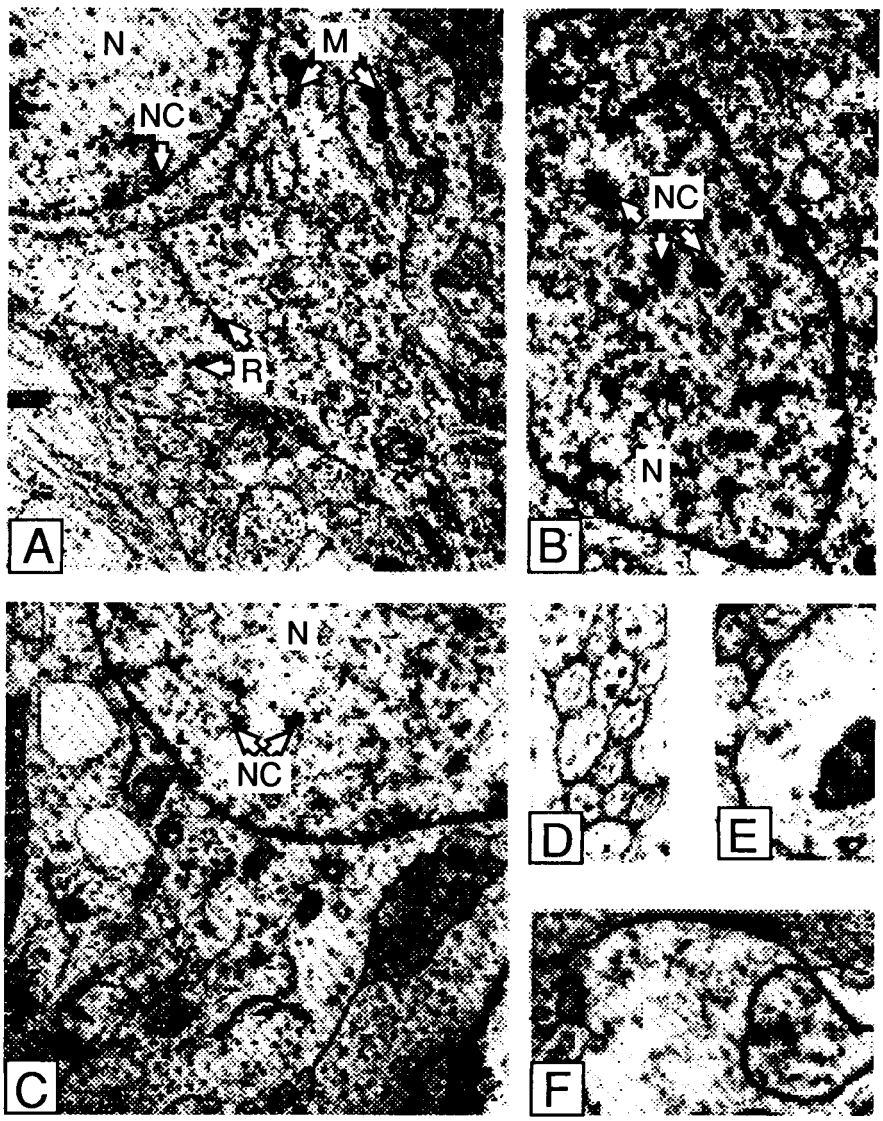



Figure 36: Ultrastructure of the bodies and axonal terminals of the neurosecretory neurons of the supraoptical nuclei of the hypothalamus of 18-day-old rat fetuses. Neurosecretory neurons of the supraoptic nuclei.
A- vivarium control X900; B - experimental group, X9000; C - synchronous group, X1100; D - axons of neurosecretory cells in the posterior lobe of the hypophysis, experimental group, X2400; E, F - axonal terminals of a neurosecretory neuron of the supraoptical nucleus in the posterior lobe of the hypophysis,, experimental group, X24,000; NN - nucleus of neurosecretory neuron; NC - nuclear chromatin; M - mitochondria; R - ribosomes

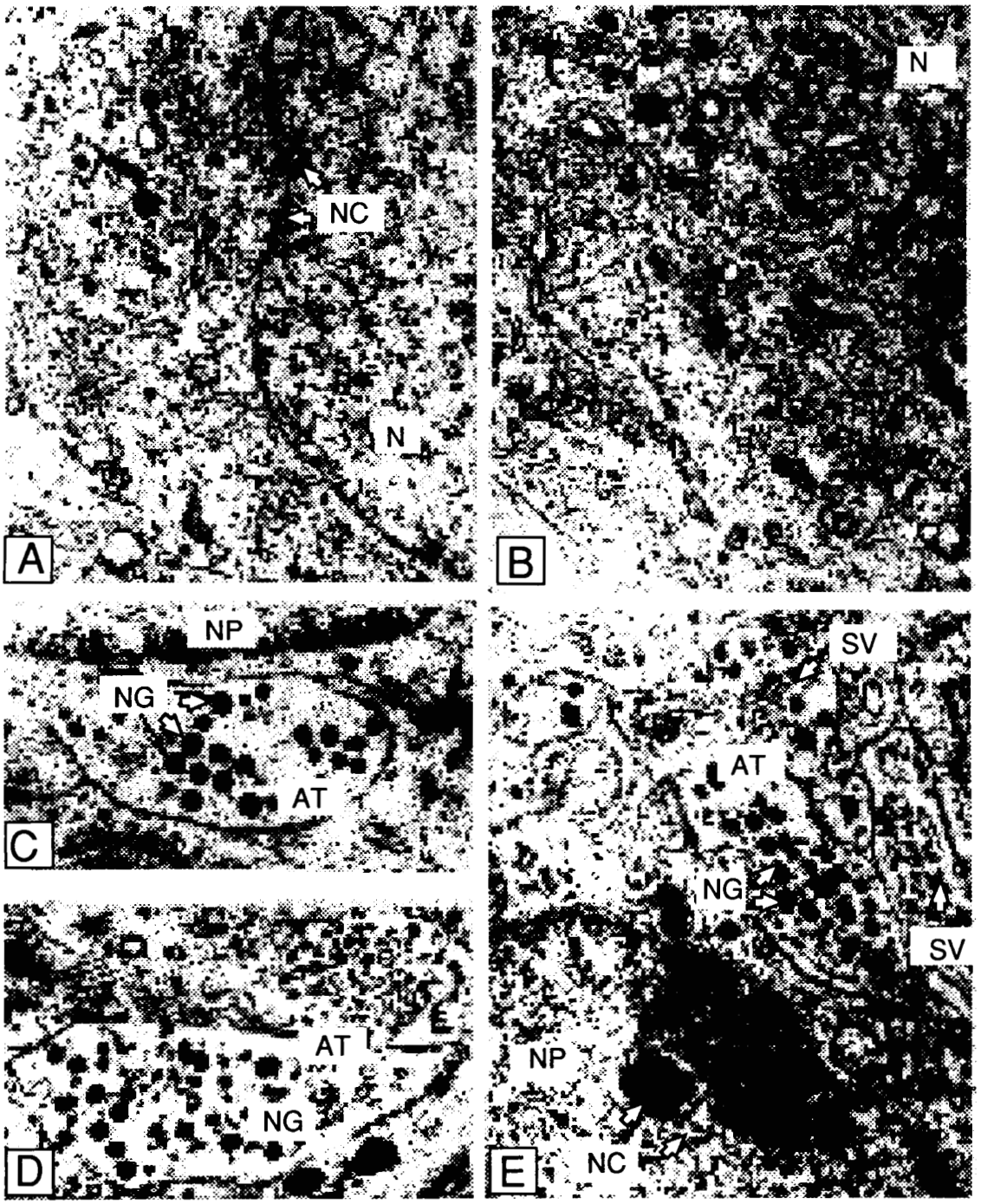



Figure 37. Ultrastructure of the bodies and axonal terminals of the neurosecretory neurons of the supraoptic nuclei of the hypothalamus of neonate rats. Neurosecretory neurons of the supraoptic nuclei.
A - vivarium control, X 12000, B - experimental group, X 900; Axonal terminal of the neurosecretory nuclei in the posterior lobe of the hypophysis: C - vivarium control, X17000, D - experimental group, X16000, E - synchronous control, X 1800, N - nucleus of the neurosecretory neuron, NP - pituicyte nucleus, NC - nuclear chromatin, AT - axonal terminal, SV - synaptic vesicle; NG - neurosecretory granules.

## OPERATIONAL MEDICINE

P1094(24/89) Grigor'yev AI, Il'in YeA, Kholin SF, Ivanovskiy YuP, Pravetskiy NV, Grushchin VI, Shakin VV.
***On the Objectives and Goals of the "Medilab"Space Medical Laboratory Project.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 21-27; 1989.
[No references]

Operational Medicine, Space Biology and Medicine
Equipment and Instrumentation
Space Flight, Mir, Medilab

Note: Because of the unusual interest of this article we have translated it in its entirety.

Text: The major result of past biomedical research in space is the demonstration that humans can be exposed to space flight for many months and still retain a rather high level of physical and mental work capacity. This successful result was made possible by the selection of cosmonauts with exemplary health and psychological stability. However, further conquest of space, the creation of permanent space stations, and future prospects for long-term flights, including a flight to Mars, will increase the complexity of the scientific research programs and require even higher levels of cosmonaut training, work capacity, and health. These factors, combined with the required expansion of the crew to admit highly qualified specialists, who may have a narrower range of adaptive capacities, make the goal of improving the existing system for medical support of space flights of primary importance.

To meet this goal it is essential that we advance to a new, qualitatively different level of biomedical research in space through performance of a broad range of comprehensive investigations. The major directions to be taken in future scientific developments include: medical support of space flight, including use of prophylactic countermeasures and psychological support; intensification of medical monitoring; provision of medical care as indicated; monitoring and control of environmental parameters in order to create optimal living conditions for the crews; study of the responses of human physiological systems and the mechanisms through which they are regulated during adaptation to space flight factors; and the study of growth, development, and evolution of biological systems under space flight conditions.

In order to solve these problems effectively, it was considered appropriate and essential to develop a dedicated biomedical laboratory for incorporation in the "Mir" space station. This laboratory would be equipped with state-of-the-art scientific research apparatus and computer technology, and would be maintained by specialists highly proficient in the area of space biology and medicine. The implementation of this project will offer the following advantages for the development of a future program of biomedical research in space: a) expansion of the range of apparatus and methodologies that can be used in space; b) improvement of the quality and increase in the number of studies performed in the medical laboratory, due to the presence of a physician and physiologist on board the medical laboratory; c) improvement of the design and regularity of the schedule for studies involving repeated measurements over time; d) opportunity for information to be processed on board in real time for on-line adjustment of the research programs; e) formation of a data bank that supports predictions concerning the needs of the current flights and, also, planning of future flights and their medical support.

The planning of biomedical programs and the prioritization of research directions will be conducted as a logical continuation and enhancement of previous research, taking into account previous experience in clinical medicine, normal physiology, and biology.

The proposed set of medical, physiological, psychophysiological, biochemical, and biological investigations on board the biomedical laboratory makes it possible to develop, select, and utilize scientifically justified approaches, methods, and devices for:

- diagnosis and treatment of diseases developing during space flight;
- monitoring and control of the environment;
- prevention and correction of the effects of space flight factors;
- control of vital process during space flight;
- identification of the reserve capacities of the body, and increased accuracy in determining the optimal duration of human exposure to space;
- study of the characteristics of interactions within a man-machine system under space flight conditions.

A hierarchical diagram of the objectives and goals of the "Medilab" project is presented in Figure 1.

Successful accomplishment of these goals will enable us to improve the existing system for supporting human work capacity and health at an optimal level during space flight and to raise them to a qualitatively new level. In addition, it follows from analysis of the contemporary state and prospects for development of space biology and medicine, that the countries and international organizations that have taken the lead in the conquest of space are already planning to create dedicated biomedical laboratories as components of space stations. The creation of dedicated orbital biomedical laboratories will facilitate the further progress of manned cosmonautics, and also public health.

**Purpose.** The dedicated "Medilab" orbital laboratory must allow:

- conduct of increased medical monitoring of the crew of the orbital space station (including during EVAs), prophylactic, and therapeutic-diagnostic measures (including emergency aid as indicated), psychological prophylaxis, and psychological support.
- monitoring and control (cumulative and on-line) of the environment, use of measures to improve sanitary and hygienic conditions on the "Mir" space station;
- deployment of a set of state-of-the-art prophylactic, therapeutic and diagnostic, and scientific research apparatus;
- systematic conduct of biomedical investigations;
- simultaneous implementation of several special purpose programs (Figure 2);
- optimization of collection and analysis of data on board the laboratory with the aid of systems for processing biomedical information;
- on-line communication and exchange of information with the ground-based medical monitoring station;
- continuous participation of two highly qualified and specially trained physicians.

The design of the interior of the orbital laboratory, along with the function, composition, and outfitting of the modules with scientific research apparatus, must provide optimal work conditions for the specialists and facilitate effective implementation of the research programs, taking into consideration the latest findings and requirements in the sphere of ergonomics.

The design of "Medilab" must provide protection from external space flight factors within acceptable limits established for manned vehicles.

The large number of scientific and practical countermeasures planned for use on board "Medilab" necessitates the presence of a clinical physician and physiologist. Before "Medilab" begins to operate, the physician must pass through the period of adaptation to weightlessness in the base module of the station (7 days minimum), during which time he will have performed medical examinations of the crews. Replacement of operators on "Medilab" must occur no more frequently than once every 3 months (after the completion of the 3-month program cycle). Here the crew that has finished its shift will return to Earth no sooner than 7 days after the arrival of the replacement crew. This time interval is needed to enable comprehensive examination of the newly arrived cosmonauts during their period of acute adaptation to weightlessness, and also to allow physicians on the new crew to become familiar with the progress of the ongoing experiments and the major results of the work already performed.

The "Medilab" operators will sleep and eat with the crew of the "Mir" station.

The design of "Medilab" stipulates the presence of its own life support systems, including a system for maintaining the gaseous composition of the atmosphere and a system for maintaining thermal conditions.

**Design.** The design of "Medilab" must provide for the division of the interior space into four compartments (Figure 3): 1) the transfer compartment, 2) the scientific research compartment, 3) the therapeutic-prophylactic compartment, 4) the biological research compartment.

**Transfer compartment.** The transfer compartment adjoins the docking port of "Medilab" and allows cosmonauts to pass from the "Mir" station into the scientific research compartment. The major portion of the service systems and the recesses and cabinets for storing the reserve inventory and instrumentation are located in the transfer compartment.

**Scientific-research compartment.** The scientific research compartment is intended for conducting intensive medical monitoring of the health status of the space station crew, and also for research on the state of the regulatory mechanisms of human physiological systems with the goal of developing and improving methods and means for medical support of space flight, as well as supporting an optimal level of work capacity in cosmonauts. The compartment is to be located in the middle portion of the orbital laboratory, between the transfer compartment and the therapeutic-prophylactic compartment. This compartment houses the major portion of the scientific research apparatus, the system for processing biomedical information and also the system for creating artificial gravity (centrifuge). Its design must allow the physicians free access to the scientific research apparatus and experimental set-ups when research is in progress. The scientific research apparatus and also the equipment for processing biomedical information must be positioned around the periphery of the compartment in clusters of equipment racks using a common system of mechanical, power, and information switching, providing maximum configuration density and allowing efficient servicing of the apparatus. For efficient servicing of the apparatus during research activities, individual units, devices, and instruments will be configured in the following equipment racks:

- for research on the cardiovascular system, including blocks for recording vascular pressure and parameters of central and regional hemodynamics using ultrasound, electrophysiological, and radioisotope methods, etc.;

- for research on the functions of external respiration and gas-energy metabolism, including mass spectrometers, blocks for measuring pressure, volume, and flow of gases, tanks with gas mixtures, a meter for measuring acid-base composition of blood, etc.;

- for research on the central nervous system and sensory systems using electrophysiological methods, including amplifiers of biological potentials and electrostimulators.

The scientific research compartment also will house equipment for preventing the effects of weightlessness and performing physical conditioning exercises. This will include easily set-up, portable bicycle ergometers, a treadmill, a system for breathing under excess pressure, a neurophysiological chair, etc. The compartment will contain the first work station for the physician, to be used for monitoring progress of research performed in the scientific research compartment and the therapeutic prophylactic compartment, and also for on-line and retrospective analysis of information through interaction with the on-board computers and for formatting information flow between "Medilab" and the ground-based medical control station. The work station will be equipped with an adjustable operator's chair, a display with a keyboard, a graphic printer, an operator's console with a three-coordinate manual control, a video tape recorder with a recording videocamera, and a device for outputting and recording information on magnetic tapes.

**Therapeutic-prophylactic compartment.** The therapeutic prophylactic compartment is designed for diagnosing state of health, utilizing prophylactic countermeasures, and providing medical care. In addition, there are plans to conduct biochemical and psychophysiological research here, and to utilize psychoprophylactic measures to maintain a high level of cosmonaut work capacity. This compartment is located between the scientific research compartment and the biological research compartment, and is separated from the former by removable partitions and from the latter by fixed partitions.

The therapeutic prophylactic compartment is to consist of three functional zones.

Zone A will be used for diagnosing cosmonauts' state of health and for provision of medical care as indicated. It should contain a portable, folding table, a chair for the patients, and anesthesiological and resuscitation devices. The required instrumentation and diagnostic kits will be stored in special recessed cabinets arranged according to functional designation. Above the table and chair there must be a shadow-free (diffuse?) lamp for illuminating the operating field (at intensity no less than 500 lux). Zone A will also contain a portable X-ray machine, physiotherapy apparatus, and a bactericidal lamp.

Zone B will be used for taking blood and performing biochemical analyses. It must contain a removable stall for taking blood samples and a rack containing the biochemical analysis blocks, a pH meter, a spectrophotometer, a microscope, refrigerators, thermostats, centrifuges, containers for storing reagents, etc.

Zone C will be used for performing psychophysiological research and implementing psychoprophylactic countermeasures. It will contain the second work station for the physician or operator and will be similar to the first physician's work station in the scientific research compartment. For implementation of psychoprophylactic measures, it will also be configured with an electroacupuncture diagnostic and treatment unit, apparatus for biofeedback sessions,

generators of odors and ions, an ozonizer, a slide projector, and removable wall screens for projecting colored images to optimize the environment, and also a photophonic stimulator (light and sound generator). The second physician's work station must provide voice contact between the cosmonauts and the Earth along a closed duplex channel.The removable partitions will allow the scientific research and therapeutic-prophylactic compartments to be combined into a single space.

**Biological research compartment.** The biological research compartment will be used for performing fundamental research to study the growth, development, and evolution of living systems under space flight conditions, and to determine the general biological and genetic consequences of long-term exposure of living systems to microgravity. This biological research compartment will be located in the distal portion of the orbital laboratory and will be accessible to the scientific research and therapeutic-prophylactic compartments through a side passage.

The biological research compartment will house:

- a set of apparatus for hermetically sealed maintenance of 50 rats, with automated delivery of food, collection of wastes, regulation of temperature and illumination, and telemetric recording of animals' motor activity, body temperature, heart rate, and blood pressure;

- a biological rack, including thermally stabilized containers for research on cultures of plant and animal cells, plants, and insects,a freezer, a unit for obtaining and fixing biological materials (glove box), and a centrifuge;

- a work station for the physician-researcher, equipped with a microscope with a video attachment, a device for sacrificing the animals and performing surgical operations;

- a biochemical analyzer;

- special recesses for storing auxiliary equipment and chemical reagents.

The design for the devices for maintaining and operating on the biological subjects and materials must provide the maximum possible hermetic isolation of the areas in order to prevent their interaction with the environment of the biological research compartment. Special filters will be installed at the input and output points of the compartment's air circulation system to provide supplementary cleaning from trace contaminants and also bacterial and odor absorbing filters.

The side passage connecting the biological research compartment with the prophylactic-therapeutic and scientific research compartments must regulate pressure differentials so that when the doors are open to allow the physician to enter, air flow will be into the compartment. This passage must house a special chamber (lock) for waste disposal of processed biological material, single use sensors, personal hygiene material, etc., and also a lavatory facility for use while working in "Medilab."

All "Medilab" compartments must be equipped with videotelephone systems and intercom communication with the space station and Earth.

**Mathematical support.** For the first time in the practice of space biology and medicine, in all phases of the "Medilab" project, information processing and computer technology will utilize a completely new integrated quantitative procedure for collecting and drawing conclusions from

data and observations. This procedure makes comprehensive use of modern information processing technology -- "data base engineering," systems analysis and mathematical modeling.

As early as the preliminary ground-based stage of the "Medilab" project, work was begun to draw conclusions from and organize data obtained previously from earlier scientific research programs; to collect hypotheses, mathematical models, biomedical theories, and also scientifically derived practical recommendations and decisions (including draft decisions on the "Medilab" project) based on previous observations and to systematize them in an integrated quantitative form. Systems analysis of existing knowledge and program goals will make it possible to plan and justify the objectives of further research, to determine what is needed,including specifications for scientific apparatus and the extent to which it must be automated, as well as specifications for the system for processing biomedical information, software and information processing support for"Medilab." The additional mathematical treatment and systematization of the available data and information will constitute a type of mathematical modeling of future research programs under ground-based conditions. This treatment, supplemented by the expert evaluations of specialists and taking into account the strengths and weaknesses of previous programs, will make it possible to refine the planned subprograms of biomedical research, coordinate their experimental schedules, and optimize these schedules so as to obtain the maximum information at the minimum cost.

Thus, systematic utilization of computer and information processing technology during the preliminary stage of the "Medilab" project will provide the preconditions for natural and logical advance to the second stage -- experiments on board "Medilab," results of which will be processed by the same information technology (Figure 4). During this stage, this technology will not only support automated routine information processing operations involving planned (routine) research, but will also provide means to organize and classify observations and handle the increasing amount of biomedical information based on observation of the outcomes of both planned and unforeseen effects. The physician-researchers on board "Medilab" and on Earth will obtain convenient and rapid access to the data base, which will be updated and expanded in the course of the research, and to the knowledge base, which will be adjusted through the active participation of the physician-researchers and by the addition of new data in the form of hypotheses, models, and theories. The latter will provide a basis for further thinking, for continuation of routine experiments and design of new investigations, and for practical conclusions and recommendations in accordance with the questions that arise and the goals and objectives of the "Medilab" project.

The process described will be repeated cyclically until the objective of the project, modified on the basis of the changing conditions and the research performed, is attained. This event will mark the beginning of the third stage of the "Medilab" program -- shift to practical utilization on Earth of the knowledge acquired during the "Medilab" flight.

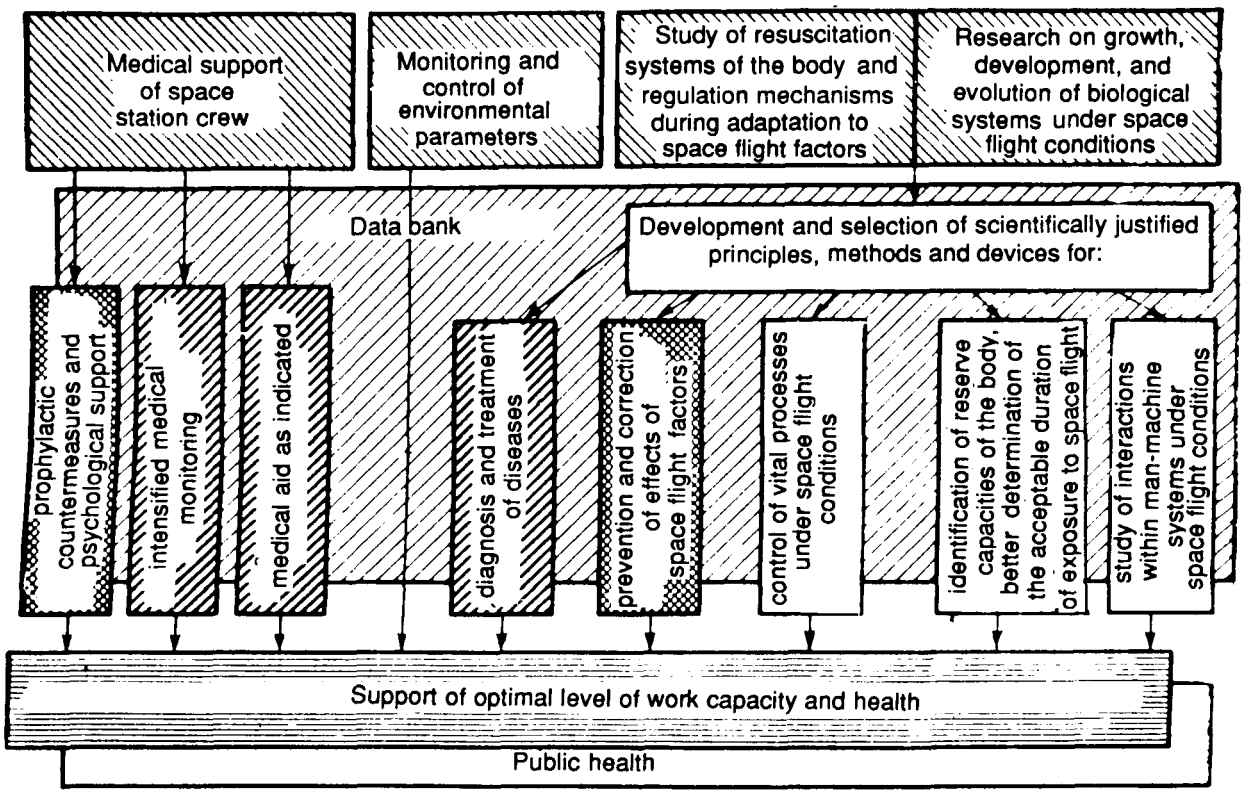



Figure 1: Hierarchical diagram of the objectives and goals of the "Medilab" project

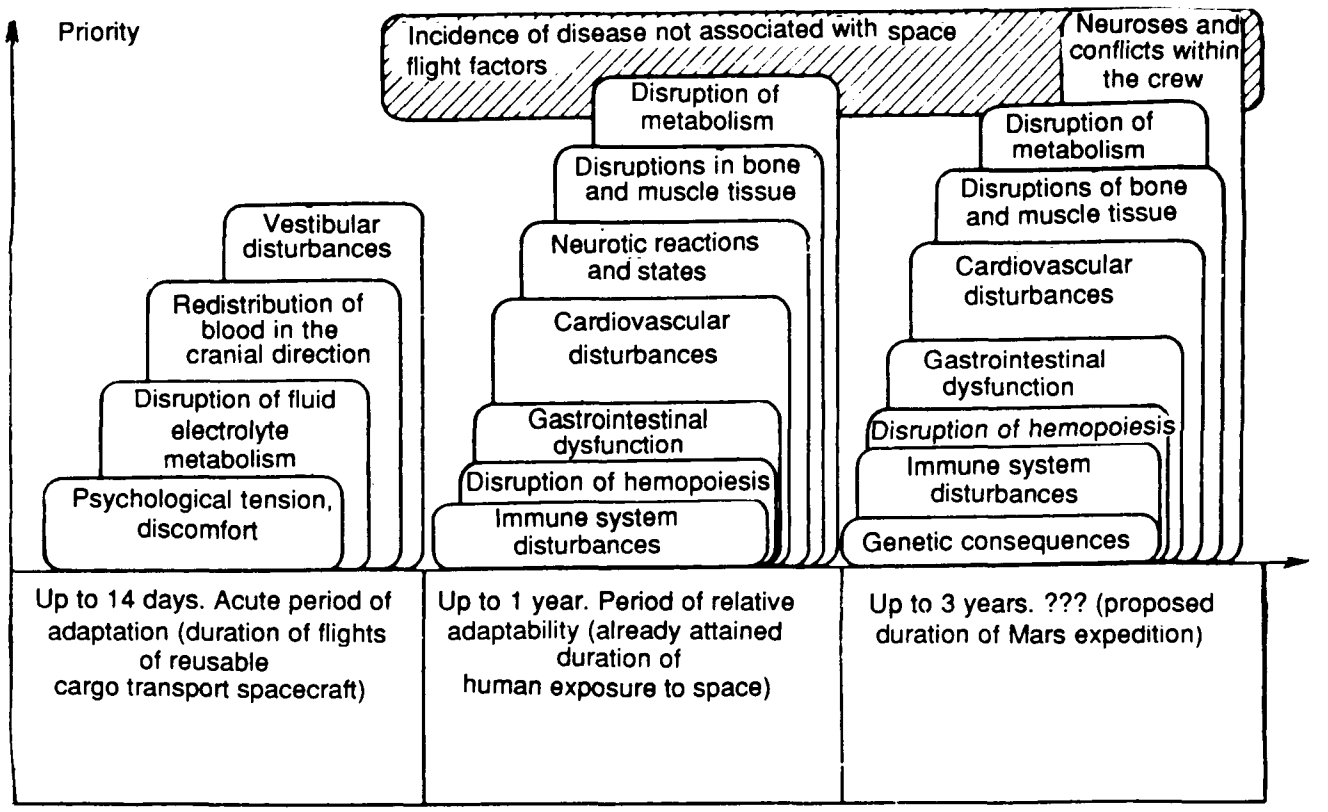



Figure 2: Possible disruptions of physiological functioning as a function of duration of human exposure to space

Figure 3. One configuration of "Medilab"

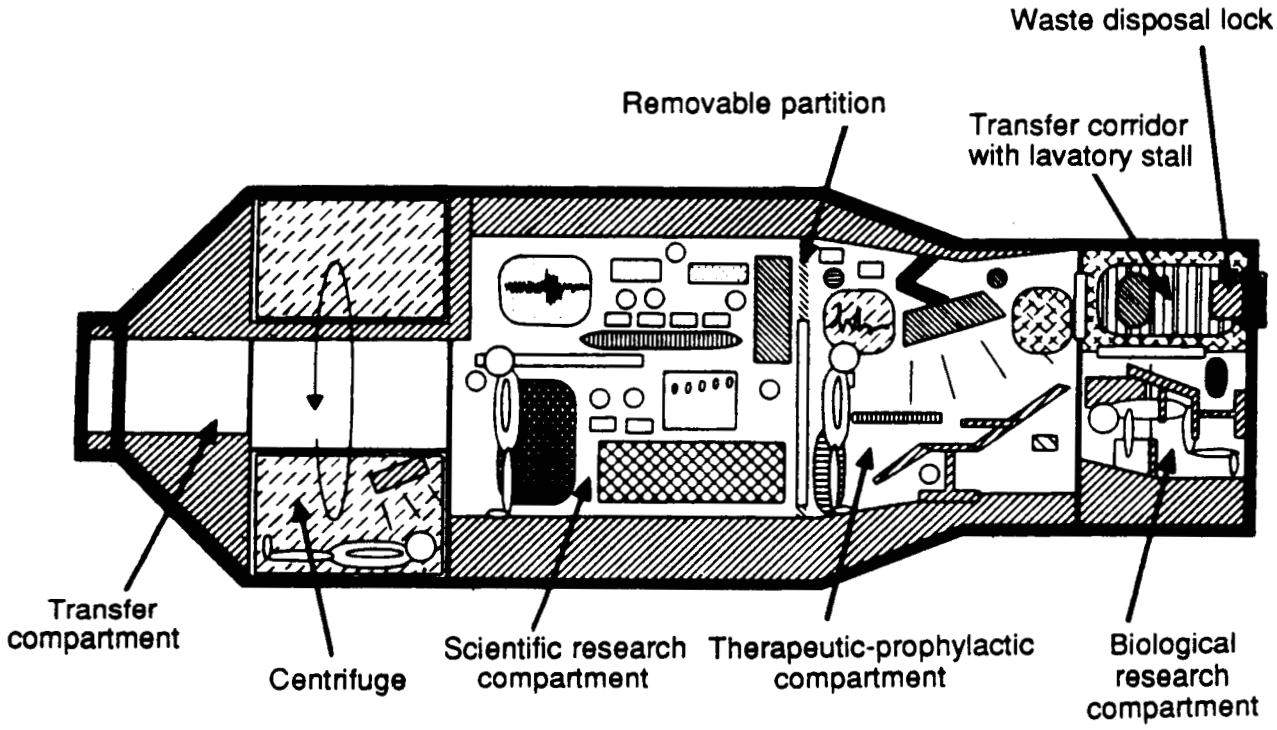
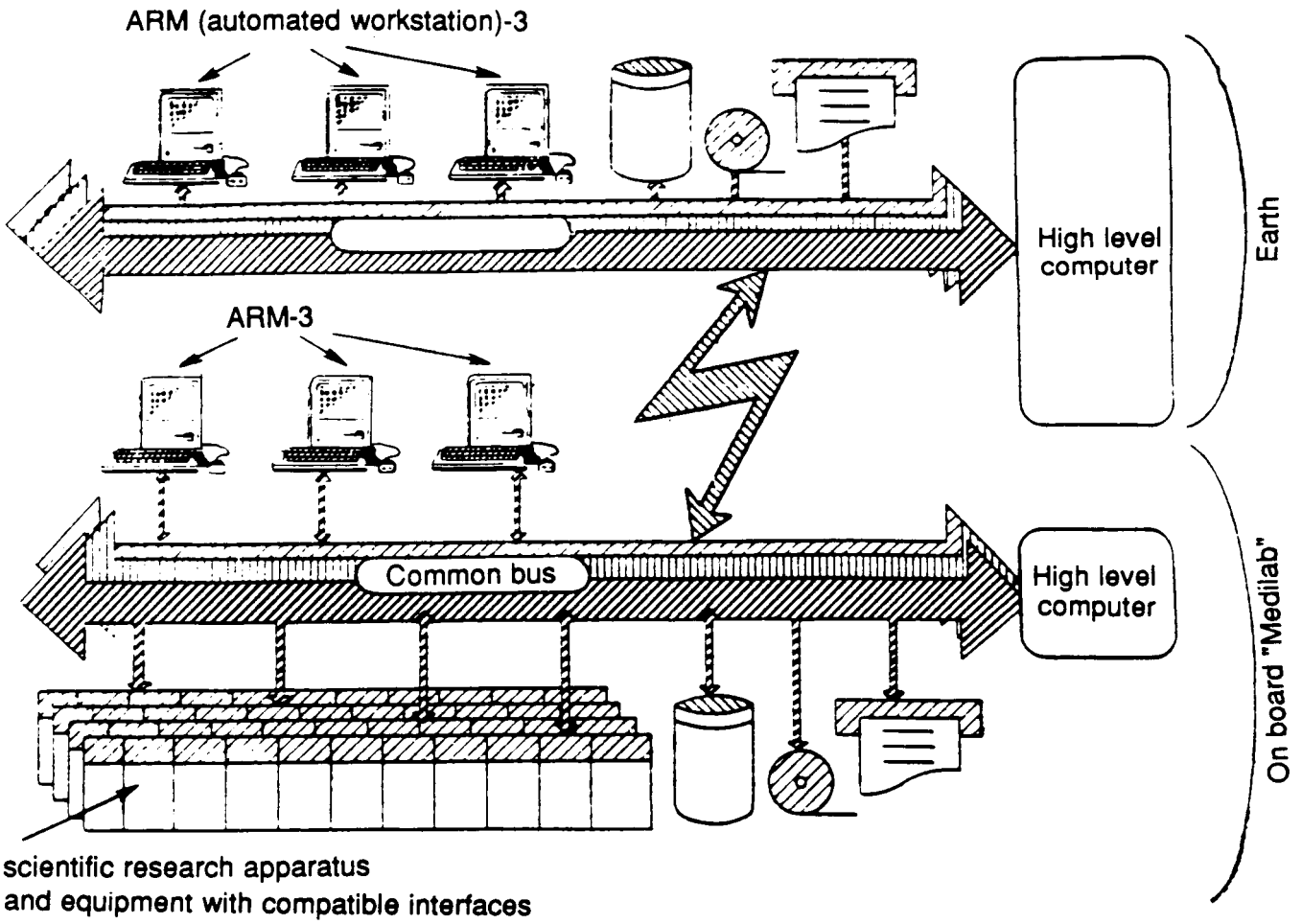


Figure 4: System for processing biomedical information



P1096(24/89) Plyasiva-Bakunina IA, Volkov VV, Kivayav AA, Kizim LD. Senkevich YuA, Solv'yev VA, Ushakov NA, Gladkikh AF, Kuz'min MP, Tkachenko VK.
***A pilot study of the use of contact lenses on long-term space flights.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
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[No references]

Operational Medicine, Contact Lenses
Humans, Cosmonauts
Space Flight, Salyut-7

Abstract: It may not be expedient to exclude individuals from space flight because of their need for corrective lenses. However, under certain conditions the wearing of glasses may be inconvenient or even impossible. In such cases contact lenses may be the solution. The study described here attempted to test the feasibility of using contact lenses on manned space flight. In particular the following issues were addressed: retention of skills in inserting and removing contact lenses in space'; retention of the lens in the eye in weightlessness; level of correction of ametropia in space; evaluation of an experimental space lens case; retention of the lens' physical properties during long-term space flight.

Two months before the beginning of space flight a soft lens was produced for a crewmember suffering from mild myopia in the right eye. The cosmonaut mastered the skills of inserting and removing the lens, as well as how to care for them. A special moisture proof container was developed which could be filled with distilled water. Two spare lenses were also developed. The container and lenses were sterilized 5 days before launch. The container was continually carried by the cosmonaut (Salyut-7 flight engineer) in the breast pocket of his flight suit. The crew captain evaluated the position of the lens and the tissue response in the right eye of his fellow crewmember. Level of correction was measured by giving a test of visual acuity in the right eye before and after a 5-hour wearing of the lens. The cosmonaut wore the lens for 5 hours at a time on days 10, 45, and 60 of a flight of Salyut-7 and once on day 30 of a Mir flight. No abnormalities were noted in association with the wearing of the lens and vision was improved. The authors conclude that they have found no evidence arguing against the use of soft contact lenses on space flights.

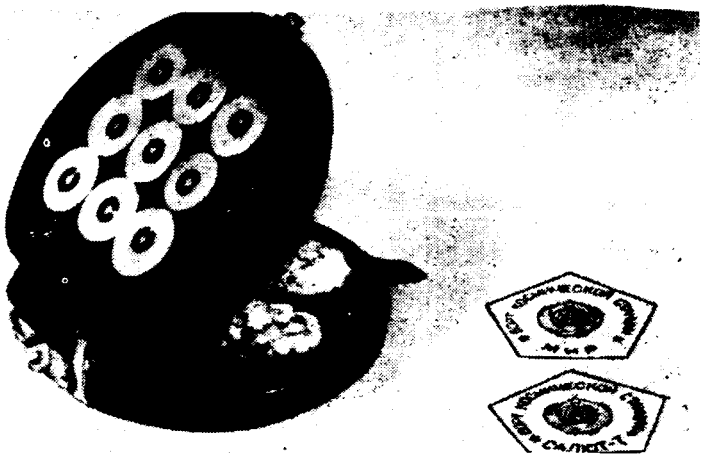

Figure 1: Container for soft contact lenses

Figure 2: Photograph of the right eye wearing a soft contact lenses on day 10 of orbital flight.

P1099(24/89) Panferova NYe, Anisimova IV, Pavlova LS, Polyakov VM.
***A study of core temperatures in healthy humans undergoing hypokinesia.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 42-46; 1989.
[11 references; 4 in English]

Operational Medicine, Core Temperature
Humans
Hypokinesia with Head-Down Tilt, Long-Term; Exercise

Abstract: Experiments were performed on 10 healthy males undergoing hypokinesia (-5°) 45-50 days in duration. One group of 5 subjects engaged in exercise during treatment, while the second group did not. Temperature was measured in surface tissues with an electric thermometer, with a point thermoprobe-thermistor, and in deeper tissues at the same points using a specially-developed radiothermometer. Temperature was measured at the following points on the right side of the body: on the back of hands and feet; along the midline of the surface of the forearm and shoulder 10 cm above and below the elbow; along the midline on the lateral surface of the calf and thigh 20 cm above and below the knees; on the skin of the forehead 1 cm above the eyebrow; on symmetrical portions of the skin of the chest along the midline of the clavicle at the level of the fifth intercostal and the stomach 5 cm above the nipple; on symmetrical portions of the skin of the head and parietal area. Subjects were dressed in shorts and air temperature was 21-23° c. Baseline measurements were made on subjects in a horizontal position. Before the measurements axillary temperature was recorded.

In the baseline period no substantial intergroup differences were noted in skin or core temperatures. Core temperatures were higher than skin temperatures at all points With the exception of the head, both skin and core temperatures dropped as distance from the heart increased. Core temperatures showed smaller limb - chest differences and greater head-chest differences. Exposure to hypokinesia with head-down tilt decreased skin temperature in all points in both groups, but to a more pronounced extent in group 2 (no countermeasures). In group 2, core temperatures decreased somewhat in the hand, foot, and forearm and remained the same in other regions. In group 1, core temperature tended to increase. Body temperature remained virtually unchanged in both groups. Skin-core differential increased in both groups.

Table: Patterns of temperature change in various points of the human body according to data from electro- and radiothermometry before and on day 50 of hypokinesia with head-down tilt

Figure: Skin and core temperatures in subjects during the baseline period

P1102(24/89) Filipenkov SN.
***Probability of decompression sickness in tests of high altitude suits.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 53-58; 1989.
[11 references;3 in English]

Operational Medicine, Decompression Sickness
Humans, Males
Equipment and Instrumentation, High Altitude Suits, Exercise

Abstract: A total of 193 male volunteers (mean age 28), who had been medically certified as healthy and showed good endurance of moderate hypoxia and low barometric pressure, participated in barochamber studies. Altitude decompression sickness was diagnosed on the basis of subjects' reports and objective clinical symptoms. Severity was classified according to the following scale: I — transient or weak sensations of discomfort; II — moderate sensation of pain not preventing performance of physical work; III — intense pain precluding possibility of work; IV — distress requiring immediate medical aid. In the studies, subjects exposed to the low pressure were either in a state of relative rest, performed tasks using equipment with mean hourly expenditure of energy of 100 calories, or performed graded physical exercise. The tasks were performed either sitting or standing and involved: manual and pedal control simulating piloting tasks, with hourly energy expenditure of 150-200 calories and work periods of 5-20 minutes alternating with rest periods of 3-30 minutes; stepping on and off a step or walking in place, involving hourly expenditure of 200-300 calories, with work periods of 10-50 minutes alternating with periods of 10-30 minutes of rest. Decompression schedules were equivalent to those used in testing of high altitude suits. Conditions and their results are presented in Table 1.

The authors conclude that the reliability of the majority of decompression schedules designed for long-term work under conditions of low barometric pressure after 1-2 hours breathing of oxygen under normal pressure is 75% to 90%. Only under conditions of short-term decompression with a coefficient of saturation of 3.3 to 5.4 did reliability increase to 90-98%. When the coefficient of saturation was 1.9-2.1, 0.5-1 hour breathing of oxygen prevented development of decompression sickness, providing 98-99% reliability under conditions of strenuous physical work. Use of 1-6 hours desaturation with pressure lowered to 40-41 kPa was effective only when physical activity was moderate and exposure to pressure of 26-29 kPa was relatively brief (up to 15 minutes). Under these conditions reliability was 95-98%.

Table : Frequency of altitude decompression sickness in subjects wearing altitude suits

| Cond. | Press. in suit, mm Hg | Desat hrs/mm Hg. | Energy expen Cal/hr | Peak Cal/min | Cases | Number Subjs | ADS | Time, minutes Expers | to ADS |
|---|---|---|---|---|---|---|---|---|---|
| I 1 | 300-320 | 40%$O_2$, 60%$N_2$ | 150 | 4 | 137 | 34 | 2 | 60-125 | 20-55 |
| I 2 | 300-320 | 95%$O_2$, 5%$N_2$ | 150 | 4 | 103 | 62 | 0 | 60-125 | |
| I 3 | 267 | 95%$O_2$, 5%$N_2$ | 150 | 4 | 28 | 18 | 0 | 60-240 | |
| I.4 | 280-290 | 0.5/550 | 300 | 8-14 | 224 | 55 | 0 | 180-360 | |
| I.5 | 280-290 | 0.8/550 | 250 | 6-10 | 12 | 6 | 0 | 180-360 | |
| I.6 | 280 | 1/760 | 150-200 | 4-6 | 6 | 6 | 0 | 180-240 | |
| I.7 | 197-214 | 2-4/280 | 250-300 | 6-10 | 59 | 42 | 3(2) | 15 | 1-12 |
| II.8 | 197-214 | 5-6/280 | 250-300 | 6-10 | 42 | 20 | 2(1) | 15 | 1-2 |
| II.9 | 197-214 | 2-3/280 | 200-250 | 6-10 | 8 | 4 | 0 | 15 | |
| II 10 | 197-214 | 1-2/300 | 150 | 4 | 53 | 31 | 0 | 15-30 | |
| III 11 | 160-175 | 1/760 | 150 | 3-5 | 22 | 20 | 0 | 5-10 | |
| III 12 | 160-175 | 1/760 | 150 | 3-5 | 12 | 9 | 2 | 60-180 | 7-35 |
| III.13 | 145-166 | 3-4/308 | 150 | 3-5 | 18 | 18 | 2 | 300-600 | 40-240 |
| III.14 | 145-166 | 1-2/760+2-4/308 | 200 | 4-6 | 9 | 8 | 2 | 120-600 | 6-30 |
| IV 15 | 145 | 0.25/760+0.5/550 | 150 | 3-5 | 17 | 13 | 0 | 3-5 | |
| IV.16 | 145 | 0.25/760+0.5/550 | 150 | 3-5 | 5 | 5 | 3 | 120 | 7-104 |
| IV.17 | 145 | 1/760 | 150 | 3-5 | 202 | 112 | 0 | 3-10 | |
| IV 18 | 145 | 1/760 | 150 | 3-5 | 56 | 39 | 4 | 30-60 | 5-14 |
| IV 19 | 145 | 1/760 | 150 | 3-5 | 27 | 20 | 5(4) | 120-240 | 5-140 |
| IV 20 | 145 | 1/760 | 150 | 3-5 | 19 | 19 | 1 | 300-600 | 270 |
| IV.21 | 145 | 2/760 | 150-200 | 4-6 | 13 | 13 | 1 | 120-240 | 180 |
| V 22 | 120-135 | 1/760 | 150 | 2-4 | 45 | 23 | 1 | 3-20 | 2.5 |
| V 23 | 105-115 | 1/760+0.5/405 | 100 | 2 | 62 | 30 | 1 | 1-4 | 2 |

Table: Distribution of symptoms of high altitude decompression according to severity, initial localization and pressure at which they occur

P1103(24/89) Chadov VI, Iseyev LR.
***Variation in the maximum acceptable coefficient of supersaturation during altitude decompression.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 58 -62; 1989.
[7 references; none in English]

Operational Medicine
Humans, Males
Altitude Decompression, Coefficient of Supersaturation, EVA Simulation

Abstract: This paper describes a series of barochamber experiments primarily directed at empirical verification of the safety of certain altitude decompression schedules. These schedules simulate various regimens for transition from the atmosphere of a space station into the oxygen atmosphere of the EVA suit with diminished working pressure. Participants in the experiments were male volunteers, aged 21-47. Nine experiments were run. With the exception of the first two, each consisted of three stages — two preliminary stages and one main stage. The first preliminary stage involved simulation of possible conditions in a spacecraft cabin immediately after launch, and involved a 2-hour exposure of subjects to an air medium with a total pressure of 840 mm Hg. The second preliminary stage simulated cabin conditions during the first few days of a space flight with diminished total pressure and normal partial oxygen pressure. Normoxic hypobaric conditions were created by generating a moderately rarified atmosphere with an elevated concentration of oxygen. This stage lasted 24 hours. The subjects performed no special physical work during the two preliminary stages. The main stage of the experiment simulated the working conditions of an individual wearing a space suit with a variety of working pressures. During this stage, which lasted 6 hours, the volunteers breathed a mixture consisting of 95% $O_2$ and 5% $N_2$. The face portion of a gas mask was used to deliver the mixture. Throughout this stage the subjects periodically (66% of the time) performed manual work with an energy expenditure of 4-6 calories/min. Decompression sickness was diagnosed on the basis of the subjects' reports and observed clinical symptoms. The $N_2$ partial pressure in alveolar gas was taken to be the baseline partial $N_2$ pressure in tissues. A total of 70 subjects participated in 383 trials.

The first two experiments were designed to establish the minimal residual pressure to which a subject previously breathing gas at normal barometer pressure can be exposed safely without preliminary desaturation. A pressure equivalent to 6300 m (454 gPA) with coefficient of supersaturation of 1.661 induced symptoms twice in 28 trials with 19 separate subjects. A pressure equivalent to 6080 m (467 gPa) and coefficient of saturation of 1.608 did not lead to decompression sickness in 51 trials with 31 separate subjects. The minimal value was considered to be 1.608. The third experiment tested for decompression sickness when subjects moved from a normoxic hypobaric medium (total pressure 733 gPa, 30% oxygen) to a lower level of residual pressure corresponding to 9320 m (293 gPa). No symptoms occurred in 69 trials with 37 separate subjects. In experiment four, subjects moved from pressure of 678 gPa to 260 gPa (equivalent to 10,100 m). As was the case in the third experiment, coefficient of supersaturation was 1.6. Of 23 trials with 22 subjects, 3 instances of decompression sickness were noted, indicating that coefficient of supersaturation is not the only parameter determining safe decompression. The fifth experiment attempted to determine the final pressure for which decompression from the initial atmosphere used in experiment four would be safe. The two subjects developing symptoms in experiment four, safely completed two and three trials with final pressure of 268 gPa. Ten other subjects underwent these conditions with no symptoms. It was determined that for a residual pressure of 268 gPa the maximum acceptable coefficient of supersaturation is 1.55. Experiments six and seven, which attempted to find the acceptable hypobaric atmosphere that would support a safe transition to a final pressure of 235 gPa, led to development of symptoms in some subjects. This suggests that,

given the maximum allowable concentration of oxygen of 40% (dictated by fire danger), shift to this pressure cannot be considered completely safe. In experiment eight, the initial pressure (560 gPa) and oxygen concentration (40%) were the same as in the previous two exxperiments, but final pressure was raised to 240 gPa. Under these conditions none of 33 subjects developed symptoms. Thus for the residual pressure of 240 gPa the maximum acceptable coefficient of supersaturation is 1.24.

The points relating coefficient of supersaturation and final pressure were plotted and a curve constructed. Experiment nine was conducted to verify the predication based on this curve. The safe value for a final pressure of 184 mm Hg was determined to be 1.42. When these conditions were empirically reproduced, no symptoms of decompression system occurred.

The authors conclude that the function relating maximum acceptable coefficient of supersaturation and final postdecompression pressure takes the form of a curve with two parts, the first of which is an almost horizontal line (for coefficient of supersaturation of 1.6 and final pressure no less than 293 gPa), while the second is a steep descending curve. In terms of altitudes, this means that for altitude equivalents of 6100-9300 m, maximum acceptable coefficient of saturation is virtually unchanged. Further increase in altitude leads to continual decrease of this coefficient.

Table: Conditions and results of experiments

Figure 1: Initial nitrogen pressure in the body as a function of total pressure of the surrounding atmosphere after decompression, reflecting the probability of development of altitude decompression sickness.

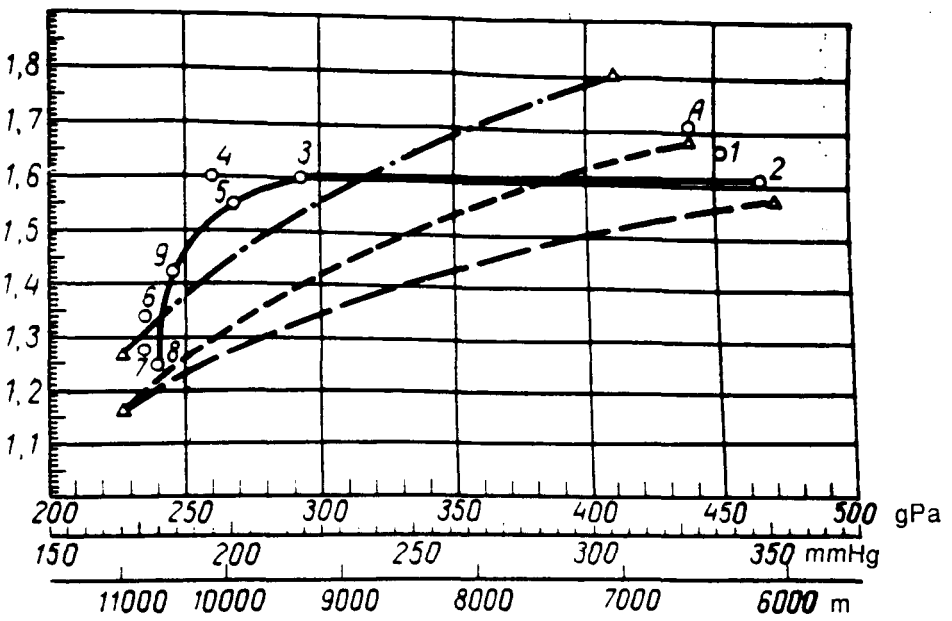


Figure 2: Coefficient of supersaturation as a function of postdecompression pressure

Abscissa: total pressure after decompression; Ordinate: coefficient of supersaturation

**PAPERS:**

P1115(24/89) Vorozhtsova SV, Yartsev Yel.
***The effect of taurine on cytogenetic damage in the cornea of mice, induced by 9GeV proton irradiation.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 89-90; 1989.
[6 references; 2 in English]

Radiobiology, Cornea; Cytology, Mitosis, Genetics, Chromosome Aberrations
Mice
Proton Irradiation, Taurine

Abstract: Experiments were performed on $F_1$ line mice irradiated with protons of energy 9 GeV at doses of 0.25 to 7.0 Gy (dose rate 0.05 Gy/sec). Some of the animals received two drops of a taurine containing solution in each eye five times before and immediately after irradiation. The solution contained 4% of the major active ingredient in taurine. The effect of this drug dosage was investigated in non-irradiated animals as a control. The efficacy of the taurine-containing solution was evaluated on the basis of frequency of formation of aberrant mitoses and change in the mitotic index after 24 and 72 hours. A total corneal preparation was made from the enucleated eyeball, stained with hematoxylin, and used to determine change in the mitotic index, number of cells, and frequency of aberrant mitoses at late anaphase and early telophase.

Irradiation led to disruption of physiological regeneration of cells in the corneal epithelium, manifest as decreased mitotic activity, and chromosomal aberrations. Decrease in mitotic index was noted soon after irradiation and decreased as dosage of radiation increased. Twenty-four hours after irradiation the eyes of the mice treated with taurine-containing solution showed an even lower mitotic index than those merely irradiated. After 72 hours these differences were not significant. When taurine solution was administered to intact animals, no effects on mitotic index were noted. As dose of irradiation increased, density of the cellular layer in the corneal epithelium measured after 24 hours decreased; taurine administration did not significantly affect this phenomenon. Frequency of aberrant mitoses was a function of radiation dose, use of taurine, and time of observation. The majority of aberrations were noted 24 hours after irradiation, after which they gradually declined. Use of taurine significantly decreased the number of cells with aberrant mitoses.

The authors conclude that taurine works by retarding mitotic activity.

Table: The effect of taurine containing solutions on the frequency of formation of aberrant mitoses in cells of the corneal epithelium at various times after irradiation by protons 9 GeV

Figure 1: Change in mitotic index in cells of the corneal epithelium of mice 24 and 72 hours after irradiation or irradiation and taurine

Figure 2: Change in number of cells in the corneal epithelium of mice 24 and 72 hours after irradiation and irradiation plus taurine as a function of radiation dose

Figure 3: Change in frequency of formation of aberrant mitoses in the corneas of mice 24 and 72 hours after irradiation and treatment with taurine

**PAPERS:**

P1111(24/89)* Baykova OB.
***Cytological study of spermatogenesis of rats exposed to hypergravity.***
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 81-82 1989.
[13 references; 7 in English]

Reproductive System, Spermatogenesis, Cytology
Rats, Males
Hypergravity, Centrifuge

Abstract: Experiments were performed on three groups of male Wistar rats, aged 3 months. Experimental (n=13), synchronous (n=7) and vivarium (n not given) control groups were used. The experimental rats were continuously exposed to hypergravity of 2-g for 5 days. Synchronous controls were housed in a cage adjacent to the centrifuge. At the end of 5 days the animals were sacrificed by decapitation and the weight of the testes, epididymis, and seminal vesicles determined. The concentration of spermatozoids was determined in a suspension of the epididymis. In smears of testes homogenate stained with azure II-eosin, spermatogenic cells were counted and classified as to stage of maturity. The following parameters were also measured:

— Sertoli index for each type of spermatogenic cell: the ratio of cells of each type to the total Sertoli cells

— spermatogenic stress — ratio of number of germ cell counted to total Sertoli cells

— percentage of multinucleated germ cells

— percentage of degenerating germ cells

Data were tested for statistical significance using Student's t.

Dissection of experimental animals revealed hyperemia of the vessels of the testes with depressed weight. Weight of the epididymus was also depressed. Mass of testicular vesicles was depressed by 9% but was not statistically significant due to large variance. Spermatozoa in 1 ml epididymal suspension was also depressed. Ratio of epididymal to testicular weight was significantly lower in the experimental group. Cytological analysis of the spermatogenic epithelium showed some difference between the experimental and control groups. The former displayed depression of relative number of spermatogons, the youngest and most sensitive cells. The index of spermatogenic stress reflected a significant decline in the total number of germ cells in the experimental group. The experimental group displayed an increase in the number of degenerating germ cells with clear pyknosis, and in the number of multinucleate cells. Since the spermatogenic cycle in rats lasts 48 days, a complete picture of the effects of chronic exposure to hypergravity on the germ, hormone-producing and trophic cells of the testes would require commensurate duration of experimental exposure to hypergravity.

P1091(24/89) Serova, LV, Denisova AM, Pustynnikova AM.
***Reproductive functions of animals spending a portion of the prenatal period under conditions of weightlessness.***
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 135-139.

Reproductive System, Reproductive Function
Rats, Males, Females
Space Flight, COSMOS-1514, Prenatal Exposure

Abstract: When animals flown on COSMOS-1514 during days 13-18 of prenatal development reached 3 months of age, their reproductive function was evaluated by breeding them with each other and with normal animals, avoiding intralitter contacts. Animals of the vivarium and synchronous control groups were bred under the same conditions. An additional group of (intact) female rats from another nursery were also used for breeding. These animals will be referred to as "intact" to differentiate them from the animals of the vivarium control which, like the animals in the other two groups, were born and raised in the vivarium of the institute. The following breeding conditions applied.

1. Males and females from the flight group were bred with each other.
2. Males of the flight group were bred with intact females.
3. Males and females of the vivarium group were bred with each other.
4. Males from the vivarium group were bred with intact females.
5. Males and females from the synchronous control group were bred with each other.
6. Males from the synchronous control group were bred with intact females.

During breeding the females were placed with the males in a ratio of 1 male to 4-5 females. Mating occurred during 2 consecutive weeks.

The results obtained are presented in Table 44. No reliable intergroup differences were found in number of females failing to be impregnated through lack of insemination or fertilization. The rather high percentage of noninseminated females in all groups may be attributed to the experimental breeding schedule, due to which some of the animals may not have been in estrous during the breeding period.

When the female rats that did become pregnant were studied, no reliable intergroup differences were found in the number of live or stillborn neonates, ratio of males to females in the litters, body weight at birth, or concentration of water and dry substance in fetal tissues. When the neonates were studied, developmental anomalies were noted in only one case (hydronephrosis and hepatic bleeding) in the litter born from interbreeding of flight animals.

Concentration of hemoglobin and leukocytes in neonates was identical in all groups. No intergroup differences were found in weight of visceral organs (liver, kidneys, myocardium, thymus, spleen) in neonate rats.

When the skeleton of the neonates was studied, no reliable intergroup differences were found in size of ossification sites in various sections of the spinal cord or girdle of the hind or front limbs, or in the bones of the skull.

During the postnatal period, no differences were found among any of the six groups in terms of body weight increase during the first month of life, or in time required for the ears to unfold or eyes to open.

It is noteworthy that in the litter obtained by interbreeding flight animals, the rate of postnatal death increased to 12%, while in the other breeding combinations there were either no deaths (four of the six groups), or one death.

It should be remembered that postnatal death rate among the siblings of the animals whose offspring died was also high (19%) compared to the vivarium and synchronous control groups. There were clear individual differences among the animals in this group. Of the four female rats in the flight group that gave birth, postnatal deaths were observed in only two mothers. Results of separate analysis of reproductive parameters for the offspring of these two groups of mothers are presented in Table 45, with control data provided for comparative purposes. Analysis of the material shows that only the litters of flight offspring whose own litters had high death rates, were marked by elevated mortality (22.2%) during the first few days of life. Other reproductive parameters were depressed in this group. Number of living neonate rats was significantly depressed, while the number of stillborn rats was elevated. The only case of developmental anomalies also occurred in this subgroup. It should be noted that reproductive capacity was studied only in females coming from high mortality flight litters; males from these litters had been used for other studies. The fact that descendants of certain mothers exposed to space during pregnancy continue to suffer reproductive impairment after at least two generations requires further study.

Hypoxia during pregnancy or prolonged birth processes has been suggested as the source of this effect, damaging the hormonal system and gonads of the fetus. Both flight mothers with high mortality litters, had difficult, prolonged labors, likely to have involved increased hypoxia and this may have led to increased postnatal death in their offspring and the latter's descendants.

Table 44: Parameters of reproductive function in animals spending a portion of the prenatal period in weightlessness.

| Group | Bred | | # Preg- | Neonates | | Males in | Postnatal | Not in- |
|---|---|---|---|---|---|---|---|---|
| | Fath. | Moth. | nant | Live | Dead | litter,% | deaths,% | seminated,% |
| 1 | F | F | 8 | 10.0±1.5 | 1.4+1.0 | 46 | 12 | 27 |
| | | | | | | | $p_{2,5}<0.01$ | |
| | | | | | | | $p_{3,4,6}<0.001$ | |
| 2 | Int | F | 5 | 9.2±.0 | 0.4±0.2 | 49 | 0 | 44 |
| 3 | VC | VC | 9 | 10.1±1.1 | 1.2±0.8 | 52 | 2.4 | 25 |
| 4 | Int | VC | 8 | 10.1±0.4 | 0.6±0.1 | 55 | 0 | 25 |
| 5 | SC | SC | 8 | 9.0±1.0 | 0.9±0.7 | 46 | 0 | 33 |
| 6 | Int | SC | 7 | 8.9±0.7 | 0 | 42 | 0 | 61 |

Table 45: Comparison of parameters of reproductive function of descendents of individual mother rats of the flight group

| Group | | # Preg- | Neonates | | Body | Anoma- | Postnatal | Not in- |
|---|---|---|---|---|---|---|---|---|
| Moth. | Fath | nant | Live | Dead | wt., g | lies, % | deaths,% | semi-nated, % |
| VC | VC | 9 | 10.1±1.1 | 1.2±0.8 | 6.0±0.12 | 0 | 2.4 | 25 |
| F:(1) | F | 4 | 13.3+0.85 | 0 | 6.1+0.16 | 0 | 4.2 | 0 |
| F:(2) | F | 4 | 6.5+1.45 | 2.8+2.1 | 5.9+0.29 | 7.7 | 22.2 | 43 |
| | | | $p<0.01$ | | | $p_V<0.05$ | $p_V<0.01$ | |

F(1) No elevated death rate in siblings.
F(2) High postnatal death rate in siblings

**BOOK REVIEW:**

BR18(24/89) ***Review of: Aviation and Space Medicine in the Third Edition of: Bol'shaya Meditsinskaya Entsiklopedia;*** Большая Медицинская Энциклопедия [Large Medical Encyclopedia].
Moscow: Sovetskaya Entsiklopediya; 1974;-1988.
Reviewed in: Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(3): 94-96; 1989.
Reviewers: Gyurdzhian AA, Nekrasov PA.

**KEY WORDS:** Space Medicine; Aerospace Medicine; Space Biology; Ecological Medicine; Human Performance; Operational Medicine

Review: In our view, the latest, third edition of the Large Medical Encyclopedia provides relatively complete, high quality coverage of issues relating to aerospace medicine.

A total of 45 special entries are devoted to aerospace medicine topics, as well as a number of sections and paragraphs in other more general articles. As a rule, specialists in aerospace medicine have participated in the compilation of such general articles (e.g., on: "The Atmosphere," "Biological Rhythms, " Hypoxia," "Hypocapnia," "Oxygen Breathing Apparatus," "Training Simulators," etc.). In addition, information relevant to aerospace medicine can be found in many articles devoted to issues of naval, submarine, occupational and sports medicine, psychological engineering, industrial hygiene, sensory physiology, the vestibular apparatus, modern research methods, biotelemetry, etc.

The close and increasingly intimate relationships between aerospace medicine and other biomedical and clinical disciplines is an important aspect of the current stage of this field's development. On the boundary between technology and medicine, aerospace medicine makes extensive use of theoretical and methodological resources of other medical disciplines. At the present time many branches of medicine are collaborating with aerospace medicine, utilizing the unique capabilities this field offers for studying unusual flight factors and the psychophysiological properties of the working conditions of flight crews, the development of life support methods, and requirements for habitability, flight certification examinations, and monitoring of the health of personnel in order to field test theoretical ideas.

In particular, many common problems exist in areas of medicine such as aviation, space, naval, and submarine. This set of disciplines can be grouped under the heading "ecological medicine," i.e., associated with the human living and working conditions in varied and frequently unusual environments. Changes in focus of interests in this area of knowledge can be to some extent traced by observing the changes in the title of the American scientific journal. At first it was called "Journal of Aviation Medicine, then "Aerospace Medicine," and now "Aviation, Space and Environmental Medicine."

The problems of aerospace medicine discussed in the encyclopedia entries can be divided arbitrarily into four groups: 1) physiological aspects of the effects of unusual flight factors on humans in the cabins of air- and spacecraft; 2) psychophysiological and ergonomic problems and also the job-related work capacity of the crew; 3) hygienic specifications of systems providing life support and ensuring flight safety; and 4) medical issues of selection, training, examination, and monitoring of the health and well-being of pilots and cosmonauts.

Rather extensive material in the third edition of the encyclopedia is devoted to the first group of problems, which we have called physiological aspects. This material includes, first of all, the traditional issues for aviation medicine of high altitude physiology (in articles on "Gaseous

composition of the atmosphere breathed," "Barometric pressure and pressure differentials," etc.), the effect of various dynamic factors (acceleration, vibration, noise, etc.), and also comparatively new factors of weightlessness, hypokinesia, and hypodynamia. These issues pertain primarily to the functions of individual organs and systems.

In our opinion, more detailed coverage should have been provided of problems belonging to the second group, which relate to the wholistic function of the human organism, the psychophysiology and job performance of the operator. The fact is that the rapid development of aerospace technology and the related increase in the complexity of the psychoemotional and intellectual aspects of the jobs of flight personnel have given rise to a corresponding shift in the center of gravity for research and scientific interest in aerospace medicine. The latter point can easily be confirmed by bibliographic references in the scientific literature.

The topics in aerospace medicine are covered mainly as sections and paragraphs within articles by specialists in other areas. This includes sensory physiology, vision ("Accommodation" and "Adaptation"), hearing, vestibular functions ("Vestibulometry," "Vestibular Apparatus, " "Vestibular Reactions," "Vestibular Sensor, " Vestibular Syndrome"), statokinetic Reactions, Coriolis Acceleration, etc.

The encyclopedia contains a number of substantive articles which cover the psychophysiological issues of job performance of flight crews: "Flights" (N.M. Rudin), "Perception During Flight" (N.D. Zavalova), "Vestibular Conditioning" (V.I. Kopanev)., "Optical Illusions," (B.S. Alyakrinskiy), "Spatial Orientation" (V.A. Ponomarenko), "Motion Sickness" (A.P. Popov). However, the majority of issues relating to the job performance of the pilot, aviation psychology, and occupational selection in aviation, psychological engineering, occupational hazards, physical training of personnel and other aspects specific to aviation are discussed only in general articles written by specialists in other areas ("Psychological Engineering," "Physical Training," "Psychology," "Statokinetic Reactions," "Occupational Hazards," etc.). Perhaps it would be beneficial to include substantive articles on issues of the psychology and psychophysiology of flight performance (for example, "Flight Performance," "Medical and Psychological Selection in Aviation," " Aviation Psychology," "Aviation Ergonomics," "Medical and Psychological Problems of Flight Safety," etc.) in the next edition. This is particularly true in light of the fact that in a number of areas (e.g., in occupational selection, and especially in safety) aviation medicine is one of the leading medical specialties. There should be more cross references to more general articles. Additionally, it would be beneficial to include all synonyms: for example, motion sickness, air sickness, space adaptation syndrome, space sickness, acute space adaptation, etc.

The third group of issues relating to hygienic problems of life support and habitability of quarters has been covered relatively fully. However, it would have done no harm to include an article on "Habitability" or "Habitability of Space and Aircraft" containing principles for standardizing environmental conditions, including workplaces and work stations.

The fourth rubric, devoted to medical support of aviation and cosmonautics, contains substantive articles on the work of flight certification boards and aviation medicine laboratories. It would have been a good idea to include a general article about the system of out-patient monitoring of the health status of flight and ground personnel, on longitudinal observations of flight personnel during the preflight period, in- and postflight, during the period between flights, and while not working, and also on medical monitoring of physical and job training, and principles underlying flight certification. It would be important here to bear in mind that aerospace medicine has acquired a great deal of expertise in these areas, which would be of interest to many areas of health care.

Aside from the groups of articles listed, the third edition of the Large Medical Encyclopedia contains substantive general articles on: "Aviation Medicine" (S.,A, Gozulov), "Space Biology" (O.G. Gazenko), "Space Radiobiology" (Yu.G. Grigor'yev), "Cosmic Radiation" (Ye.Ye. Kovalev)., and "Space Medicine" (O.G. Gazenko). Aerospace medical articles such as "Aviation Sanitation" (N.M. Rudnyy, G. M. Shereshkov) are of interest to the practice of public health. We believe that readers would have been interested in articles generalizing from the experience of aerospace medicine in the development of medical aspects of search and rescue of crews and passengers after accidents, and also on survival in extreme climatographic zones.

As in any major work, the articles contain isolated inaccuracies. For example, the article on "Aviation Medicine" implies that the headquarters of the International Academy of Aerospace Medicine is located in Paris, rather than Montreal; it is stated that the All-Union Physiological Society includes a section on Aviation and Space Medicine, which is actually a part of the I.P. Pavlov Moscow Physiological Institute.

A major virtue of the Large Medical Encyclopedia is the fact that its articles on aerospace medicine accord completely with state of the art in science, containing the most up-to-date data, and the correct relationships between theory and practice, while the interrelationships between aerospace medicine and other branches of knowledge are elucidated. The literary style in which the material is presented is irreproachable.

It is of particular note that the supplementary volume (28) contains summary articles discussing the current status and prospects of a number of crucial trends in theoretical and practical medicine. An article by O.G. Gazenko, A.I. Grigor'yev, A.D. Yegorov, and Ye.A. Il'in, entitled "Developmental Trends in Space Biology and Medicine," is worthy of particular attention. It does a fine job of describing the inception and establishment of space biology; its current status and most critical problems, and interaction with other medical, technological, and psychological disciplines; and also its role in the study of such universal human problems as "Man and Work," "Man and Technology," "Man and the Environment."

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16. Abstract

This is the twenty-fourth issue of NASA's USSR Space Life Sciences Digest. It contains abstracts of 39 journal papers or book chapters published in Russian. In addition, reviews of two recent Soviet books are translated. The abstracts in this issue have been identified as relevant to 25 areas of space biology and medicine: adaptation, aviation medicine, biological rhythms, cardiovascular and respiratory systems, cytology, developmental biology, endocrinology, equipment and instrumentation, genetics, habitability and environment effects, hematology, human performance, immunology, life support systems, man-machine systems, mathematical modeling, metabolism, microbiology, morphology, musculoskeletal system, neurophysiology, operational medicine, psychology, radiobiology, and space medicine.

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